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(54) Title: GENES INVOLVED IN TOLERANCE TO ENVIRONMENTAL STRESS

(57) Abstract

The present invention relates to a method for obtaining polynucleic acids comprising coding sequences and/or genes involved in environmental stress resistance in plants, comprising the preparation of a cDNA library comprising coding sequences from siliques, introducing said coding sequences in yeast cells in a functional format and screening for polynucleic acids leading to an enhanced tolerance or resistance to environmental stress conditions in said transformed yeast cells. The present invention further relates to an isolated polynucleic acid obtainable by such a method as listed in Table 1 as well as recombinant polynucleic acid comprising the same. The present invention further relates to an isolated polypeptide encoded by a polynucleic acid of the invention. The present invention also relates to a method for producing a plant with enhanced tolerance or resistance to environmental stress, said method comprising introducing into a plant cell a recombinant DNA comprising a polynucleic acid as defined which when expressed in a plant cell enhances the tolerances or induces resistance to environmental stress conditions of said plant. The present invention particularly relates to plant cells, plants or harvestable parts or propagation material thereof transformed with a recombinant polynucleic acid as defined above.

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Genes involved in tolerance to environmental stress

The present invention relates to molecular biology, in particular plant
5 molecular biology. In particular, the invention relates to improvements of crop productivity of useful plants. One of the major limitations of crop productivity is the effect of environmental stress conditions on plant growth and development. An important goal of molecular biology is the identification and isolation of genes that can provide resistance or tolerance to such stresses. For agriculture, the creation of
10 transgenic plants containing such genes provides the potential for improving the stress resistance or tolerance of plants.

Drought, salt loading, and freezing are stresses that cause adverse effects on the growth of plants and the productivity of crops. The physiological response to these stresses arises out of changes in cellular gene expression. Expression of a number of
15 genes has been demonstrated to be induced by these stresses (Zhu et al., 1997; Shinozaki et al., 1996; Thomashow, 1994). The products of these genes can be classified into two groups: those that directly protect against environmental stresses and those that regulate gene expression and signal transduction in the stress response. The first group includes proteins that likely function by protecting cells from
20 dehydration, such as the enzymes required for biosynthesis of various osmoprotectants, late-embryogenesis-abundant (LEA) proteins, antifreeze proteins, chaperones, and detoxification enzymes (Shinozaki et al., 1997, Ingram et al., 1996, Bray et al., 1997). The second group of gene products includes transcription factors, protein kinases, and enzymes involved in phosphoinositide metabolism (Shinozaki et
25 al., 1997). An overview of the methods known to improve stress tolerance in plants is also given in Holmberg & Bülow, (1998).

Further studies are definitely needed to give an insight into the mechanisms involved in the plant response to environmental stress conditions.

The study of plants naturally adapted to extreme desiccation has led to the
30 hypothesis that the genetic information for tolerance to environmental stress conditions exists in all higher plants. In glycophytes, this information would only be expressed in seeds and pollen grains which undergo a desiccation process.

The induction of osmotolerance in plants is very important to crop productivity:
35 30 to 50 % of the land under irrigation is presently affected by salinity. Several lines of evidence also demonstrate that even mild environmental stress conditions throughout the growth season have a negative impact on plant growth and crop productivity. It is

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for instance known that even minor limitations in water availability cause a reduced photosynthetic rate. Unpredictable rainfall, increase in soil salinity at the beginning and the end of the growing season often result in decreased plant growth and crop productivity. These environmental factors share at least one element of stress and that
5 is water deficit or dehydration. Drought is a significant problem in agriculture today. Over the last 40 years, for example, drought accounted for 74% of the total US crop losses of corn. To sustain productivity under adverse environmental conditions, it is important to provide crops with a genetic basis for coping with water deficit, for example by breeding water retention and tolerance mechanisms into crops so that
10 they can grow and yield under these adverse conditions.

It is an aim of the present invention to provide a new method for screening for plant genes involved in tolerance or resistance to environmental stress.

It is an aim of the present invention to provide new plant genes, more particularly plant genes providing the potential of improving the tolerance to
15 environmental stress conditions in plants.

It is also an aim of the present invention to provide polypeptides encoded by said new plant genes.

It is further an aim of the present invention to provide methods for producing plants with enhanced tolerance or resistance to environmental stress conditions based
20 on said new genes.

It is also an aim of the present invention to provide recombinant polynucleic acids comprising said new genes.

It is further an aim of the present invention to provide plant cells and plants transformed with said new genes.

25 It is further an aim of the present invention to provide plant cells and plants with enhanced tolerance or resistance to environmental stress conditions.

The present invention relates more particularly to a method for obtaining polynucleic acids comprising coding sequences and/or genes involved in environmental stress in plants, comprising the preparation of a cDNA library
30 comprising coding sequences from siliques, introducing said coding sequences in yeast cells in a functional format and screening for polynucleic acids leading to an enhanced tolerance or resistance to environmental stress conditions in said transformed yeast cells.

It has been found that the transfer of genes from plants which are often difficult
35 to assay for certain characteristics, to lower eukaryotes, such as yeasts and fungi, but

in particular yeast, especially *Saccharomyces*, is relatively-easy to achieve, whereby it has now been shown that the results of testing for tolerance or resistance to environmental conditions in the resulting yeast cells gives a relatively reliable measure of the capability of the inserted coding sequence or gene to induce tolerance or 5 resistance to environmental stress in plants. Thus the expression of polynucleic acid sequences comprising the gene or coding sequence which are responsible for inducing tolerance or resistance to environmental stress conditions can be enhanced in the plant species from which it originates or in any other plant species.

In the present context the term "enhancing" must be understood to mean that 10 the levels of molecules correlated with stress protection in a transformed plant cell, plant tissue or plant part will be "substantially increased" or "elevated" meaning that this level will be greater than the levels in an untransformed plant.

This may be achieved by inducing overexpression of suitable genetic 15 information which is already present, or by any other suitable means of introducing into the plant cell heterologous information resulting in a capability to tolerate or resist environmental stress.

The term "environmental stress" has been defined in different ways in the prior art and largely overlaps with the term "osmotic stress". Holmberg et al., 1998 for instance define different environmental stress factors which result in abiotic stress. 20 Salinity, drought, heat, chilling and freezing are all described as examples of conditions which induce osmotic stress. The term "environmental stress" as used in the present invention refers to any adverse effect on metabolism, growth or viability of the cell, tissue, seed, organ or whole plant which is produced by a non-living or non-biological environmental stressor. More particularly, it also encompasses 25 environmental factors such as water stress (flooding, drought, dehydration), anaerobic (low level of oxygen, CO₂ etc.), aerobic stress, osmotic stress, salt stress, temperature stress (hot/heat, cold, freezing, frost) or nutrients/pollutants stress.

The term "anaerobic stress" means any reduction in oxygen levels sufficient to produce a stress as hereinbefore defined, including hypoxia and anoxia.

30 The term "flooding stress" refers to any stress which is associated with or induced by prolonged or transient immersion of a plant, plant part, tissue or isolated cell in a liquid medium such as occurs during monsoon, wet season, flash flooding or excessive irrigation of plants, etc.

"Cold stress" and "heat stress" are stresses induced by temperatures which are 35 respectively, below or above, the optimum range of growth temperatures for a

particular plant species. Such optimum growth temperature ranges are readily determined or known to those skilled in the art.

“Dehydration stress” is any stress which is associated with or induced by the loss of water, reduced turgor or reduced water content of a cell, tissue, organ or whole plant.

“Drought stress” refers to any stress which is induced by or associated with the deprivation of water or reduced supply of water to a cell, tissue, organ or organism.

“Oxidative stress” refers to any stress which increases the intracellular level of reactive oxygen species.

10 The terms “salinity-induced stress”, “salt-stress” or similar term refer to any stress which is associated with or induced by elevated concentrations of salt and which result in a perturbation in the osmotic potential of the intracellular or extracellular environment of a cell.

15 Said salt can be for example, water soluble inorganic salts such as sodium sulfate, magnesium sulfate, calcium sulfate, sodium chloride, magnesium chloride, calcium chloride, potassium chloride etc., salts of agricultural fertilizers and salts associated with alkaline or acid soil conditions.

20 The transgenic plants obtained in accordance with the method of the present invention, upon the presence of the polynucleic acid and/or regulatory sequence introduced into said plant, attain resistance, tolerance or improved tolerance or resistance against environmental stress which the corresponding wild-type plant was susceptible to.

25 The terms “tolerance” and “resistance” cover the range of protection from a delay to complete inhibition of alteration in cellular metabolism, reduced cell growth and/or cell death caused by the environmental stress conditions defined herein before. Preferably, the transgenic plant obtained in accordance with the method of the present invention is tolerant or resistant to environmental stress conditions in the sense that said plant is capable of growing substantially normal under environmental conditions where the corresponding wild-type plant shows reduced growth, metabolism, viability, 30 productivity and/or male or female sterility. Methodologies to determine plant growth or response to stress include, but are not limited to height measurements, leaf area, plant water relations, ability to flower, ability to generate progeny and yield or any other methodology known to those skilled in the art.

35 The terms “tolerance” and “resistance” may be used interchangeably in the present invention.

The methods according to the invention as set out below can be applied to any, higher plant, preferably important crops, preferably to all cells of a plant leading to an enhanced osmotic or any other form of environmental stress tolerance. By means of the embodiments as set out below, it now becomes possible to grow crops with 5 improved yield, growth, development and productivity under environmental stress conditions, it may even become possible for instance to grow crops in areas where they cannot grow without the induced osmotolerance according to the invention.

In order to do a thorough screening for relevant plant genes and/or coding sequences, it is preferred to apply a method according to the invention whereby said 10 cDNA library comprises copies of essentially all mRNA of said plant cell. Probably only coding sequences are sufficient. For the screening of genes involved in environmental stress, it is preferred to use a cDNA library from siliques (fruits, containing the maturing seeds), such as the siliques from *Arabidopsis*, because genes involved in for instance osmotolerance are preferentially expressed in these organs.

15 Although the genetic information may be introduced into yeast for screening by any suitable method, as long as it is in a functional format long enough for testing of tolerance or resistance to environmental stress conditions, it is preferred for ease of operation to use a well known vector such as a 2 μ plasmid. It is to be preferred to have the coding sequence or the gene under control of a strong constitutive yeast 20 promoter, to enhance good expression of the gene or coding sequence of interest. Strong constitutive yeast promoters are well known in the art and include, but are not limited to the yeast TPI promoter.

The term "gene" as used herein refers to any DNA sequence comprising several operably linked DNA fragments such as a promoter and a 5' untranslated 25 region (the 5'UTR), a coding region (which may or may not code for a protein), and an untranslated 3' region (3'UTR) comprising a polyadenylation site. Typically in plant cells, the 5'UTR, the coding region and the 3'UTR (together referred to as the transcribed DNA region) are transcribed into an RNA which, in the case of a protein encoding gene, is translated into a protein. A gene may include additional DNA 30 fragments such as, for example, introns. As used herein, a genetic locus is the position of a given gene in the genome of a plant.

The present invention more particularly relates to an isolated polynucleic acid obtainable by a method comprising the preparation of a cDNA as set out above comprising coding sequences from siliques, introducing said coding sequences in 35 yeast cells in a functional format and screening for polynucleic acids leading to an

enhanced tolerance or resistance to environmental stress conditions in said transformed yeast cells.

The term "polynucleic acid" refers to DNA or RNA, or amplified versions thereof, or the complement thereof.

5 The present invention more particularly provides an isolated polynucleic acid obtainable by a method as defined above which encodes a polypeptide as listed in Table 1.

10 The capacity of an isolated polynucleic acid to confer tolerance or resistance to environmental stress conditions can be tested according to methods well-known in the art, see for example, Grillo et al. (1996), Peassarakli et al. (Editor), Nilsen et al. (1996), Shinozaki et al. (1999), Jones et al. (1989), Fowden et al. (1993) or as described in the appended examples.

15 The present invention more particularly relates to an isolated polynucleic acid which encodes a homolog of any of the polypeptides as listed in Table 1, which is chosen from:

- (a) any of SEQ ID NO 1, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, or 121, or the complementary strands thereof;
- 20 (b) polynucleic acid sequences which hybridize to sequences defined in (a) or fragments thereof;
- (c) polynucleic acid sequences which are degenerated as a result of the genetic code to the polynucleic acid sequences defined in (a) or (b), or,
- 25 (d) polynucleic acid sequences encoding a fragment of a protein encoded by a polynucleic acid of any one of (a) to (c).

Preferably said sequences according to part (b) hybridize under stringent conditions to the sequences of part (a).

30 Said fragment as defined above are preferably unique fragments of said sequences.

The term "hybridizing" refers to hybridization conditions as described in Sambrook (1989), preferably specific or stringent hybridization conditions are aimed at.

Stringent conditions are sequence dependent and will be different in different circumstances. Generally, stringent conditions are selected to be about 5°C lower than the thermal melting point (Tm) for the specific sequence at a defined ionic strength and pH. The Tm is the temperature (under defined ionic strength and pH) at which 5 50% of the target sequence hybridizes to a perfectly matched probe. Typically, stringent conditions will be those in which the salt concentration is about 0.02 molar at pH 7 and the temperature is at least about 60°C.

In the present invention, genomic DNA or cDNA comprising the polynucleic acids of the invention can be identified in standard Southern blots under stringent 10 conditions using the cDNA sequence shown. The preparation of both genomic and cDNA libraries is within the skill of the art. Examples of hybridization conditions are also given in the Examples section.

The present invention also relates to the isolated polynucleic acids which encode polypeptides which are a homolog of the polypeptides as set out in Table 1 15 useful for the production of plants which are resistant or tolerant to environmental stress conditions.

The present invention also relates to a polynucleic acid comprising at least part of any of SEQ ID NO 1, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 or 121, or 20 at least part of a gene that is at least 50% identical, preferentially at least 55%, 60%, 65% or 70% identical, more preferably at least 75%, 80% or 85% identical, and most preferably at least 90% or 95% identical to any of SEQ ID NO 1, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 or 121. Preferably, said gene encodes a protein having 25 substantially the same biological activity as the protein having the sequence of SEQ ID NO 2, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76 or 78. Said part of said gene is preferably a unique part.

The present invention preferably relates to the use of a polynucleic acid 30 comprising at least part of any of SEQ ID NO 1, 3, 5, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, or 121, or at least part of a gene that is at least 50% identical, preferentially at least 55%, 60%, 65% or 70% identical, more preferably at least 75%, 80% or 85% identical, and most preferably at least 90% or 95% identical to any of 35

SEQ ID NO 1, 3, 5, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, or 121 for the
5 environmental stress conditions.

Preferably, said gene encodes a protein having substantially the same biological activity as the protein having the sequence of SEQ ID NO 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102,
10 104, 106, 108, 110, 112, 114, 116, 118, or 120. Said part of said gene is preferably a unique part.

The present invention particularly relates to an isolated polynucleic acid as defined above, which encodes a plant homolog of yeast DBF2 kinase, more particularly a DBF2 kinase homolog from *Arabidopsis thaliana* termed At-DBF2, which
15 can at least be used to confer enhanced environmental stress tolerance or resistance in plants and yeast.

More preferably, the present invention relates to an isolated polynucleic acid encoding a plant DFB2 kinase, which is chosen from:

- (a) SEQ ID NO 1, or the complementary strand thereof;
- 20 (b) polynucleic acid sequences which hybridize to sequences defined in (a) or fragments thereof;
- (e) polynucleic acid sequences which are degenerated as a result of the genetic code to the polynucleic acid sequences defined in (a) or (b), or,
- 25 (c) polynucleic acid sequences encoding a fragment of a protein encoded by a polynucleic acid of any one of (a) to (c).

Preferably said sequences according to part (b) hybridize under stringent conditions to the sequences of part (a).

30 Alternatively, the present invention relates to a polynucleic acid derived from a plant comprising at least part of SEQ ID NO 1, or at least part of a gene having a sequence that is at least 50% identical, preferentially at least 55%, 60%, 65% or 70% identical, more preferably at least 75%, 80% or 85% identical, and most preferably at least 90% or 95% identical to SEQ ID NO 1. Preferably said gene encodes a protein

having substantially the same biological activity as the protein having the sequence of SEQ ID NO 2.

The present invention also relates to the use of an isolated polynucleic acid as defined above which encodes a plant HSP 17.6A protein for the production of transgenic plants, more particularly a homolog from *Arabidopsis thaliana*, which at least can be used to confer enhanced environmental stress tolerance in plants and yeast.

More preferably, the present invention relates to the use of an isolated polynucleic acid as defined above which is chosen from:

- 10 (a) SEQ ID NO 3, or the complementary strand thereof;
- (b) polynucleic acid sequences which hybridize to sequences defined in (a) or fragments thereof;
- (c) polynucleic acid sequences which are degenerated as a result of the genetic code to the polynucleic acid sequences defined in (a) or (b) or,
- 15 (d) polynucleic acid sequences encoding a fragment of a protein encoded by a polynucleic acid of any one of (a) to (c),

for the production of transgenic plants having an enhanced tolerance or resistance to environmental stress conditions.

Preferably said sequences according to part (b) hybridize under stringent conditions to the sequences of part (a).

The present invention also relates to the use of a polynucleic acid comprising at least part of SEQ ID NO 3, or at least part of a gene having a sequence that is at least 50% identical, preferentially at least 55%, 60%, 65% or 70% identical, more preferably at least 75%, 80% or 85% identical, and most preferably at least 90% or 95% identical to SEQ ID NO 3. Preferably said gene encodes a protein having substantially the same biological activity as the protein having the sequence of SEQ ID NO 4, for the production of transgenic plants having enhanced tolerance or resistance to environmental stress conditions.

More preferably, the present invention relates to the use of an isolated polynucleic acid as defined above which is chosen from:

- 35 (a) any of SEQ ID NO 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, or 119, or the complementary strand thereof;

10

- 5
- (b) polynucleic acid sequences which hybridize to sequences defined in (a) or fragments thereof;
 - (c) polynucleic acid sequences which are degenerated as a result of the genetic code to the polynucleic acid sequences defined in (a) or (b) or,
 - (d) polynucleic acid sequences encoding a fragment of a protein encoded by a polynucleic acid of any one of (a) to (c),

for the production of transgenic plants having an enhanced tolerance or resistance to
10 environmental stress conditions.

The present invention preferably relates to the use of a polynucleic acid comprising at least part of any of SEQ ID NO 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, or 119, or at least part of a gene that is at least 50% identical, preferentially at least 55%, 60%, 65% or 70% identical, more
15 preferably at least 75%, 80% or 85% identical, and most preferably at least 90% or 95% identical to any of SEQ ID NO 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, or 119, for the production of transgenic plants having enhanced tolerance or resistance to environmental stress conditions.

Preferably, said gene encodes a protein having substantially the same
20 biological activity as the protein having the sequence of SEQ ID NO 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, or 120. Said part of said gene is preferably a unique part.

According to another preferred embodiment, the present invention relates to an isolated polynucleic acid as defined above, which encodes a protein termed c74,
25 more particularly a plant homolog of c74, even more preferably a c74 from *Arabidopsis thaliana*, which at least can be used to confer enhanced environmental stress tolerance in plants and yeast.

More particularly, the present invention relates to an isolated polynucleic acid as defined above, which is chosen from:

30

- (a) SEQ ID NO 5, or the complementary strand thereof;
- (b) polynucleic acid sequences which hybridize to sequences defined in (a) or fragments thereof;

- (c) polynucleic acid sequences which are degenerated as a result of the genetic code to the polynucleic acid sequences defined in (a) or (b) or,
- (d) polynucleic acid sequences encoding a fragment of a protein encoded by a polynucleic acid of any one of (a) to (c).

5 Preferably said sequences according to part (b) hybridize under stringent conditions to the sequences of part (a).

10 The present invention also relates to a polynucleic acid comprising at least part of SEQ ID NO 5, or at least part of a gene having a sequence that is at least 50% identical, preferentially at least 55%, 60%, 65% or 70% identical, more preferably at least 75%, 80% or 85% identical, and most preferably at least 90% or 95% identical to SEQ ID NO 5. Preferably said gene encodes a protein having substantially the same biological activity as the protein having the sequence of SEQ ID NO 6.

15 Two nucleic acid sequences or polypeptides are said to be "identical" according to the present invention if the sequence of nucleotides or amino acid residues, respectively, in the two sequences is the same when aligned for maximum correspondence as described below. The term "complementary to" is used herein to mean that the complementary sequence hybridizes to all or a portion of a given 20 polynucleotide sequence.

Sequence comparisons between two (or more) polynucleic acid or polypeptide sequences are typically performed by comparing sequences of the two sequences over a "comparison window" to identify and compare local regions of sequence similarity. A "comparison window", as used herein, refers to a segment of at least 25 about 20 contiguous positions, usually about 50 to about 200, more usually about 100 to about 150 in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted by the local homology algorithm of Smith and Waterman (1981), by the homology alignment 30 algorithm of Needleman and Wunsch (1970), by the search for similarity method of Pearson and Lipman (1988), by computerized implementations of these algorithms (GAP, BESTFIT, BLAST, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group (GCG), 575 Science Dr., Madison, WI), or by visual inspection.

"Percentage of sequence identity" is determined by comparing two optimally aligned sequences over a comparison window, wherein the portion of the polynucleic acid or polypeptide sequences in the comparison window may comprise additions or deletions (i.e., gaps) as compared to the reference sequence (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid base or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the window of comparison and multiplying the result by 100 to yield the percentage of sequence identity.

The term "substantial identity" of polynucleic acid or polypeptide sequences means that a polynucleotide sequence comprises a sequence that has at least 60%, 65%, 70% or 75% sequence identity, preferably at least 80% or 85%, more preferably at least 90% and most preferably at least 95 %, compared to a reference sequence using the programs described above (preferably BLAST) using standard parameters. One of skill will recognize that these values can be appropriately adjusted to determine corresponding identity of proteins encoded by two nucleotide sequences by taking into account codon degeneracy, amino acid similarity, reading frame positioning and the like. Substantial identity of amino acid sequences for these purposes normally means sequence identity of at least 40%, 45%, 50% or 55% preferably at least 60%, 65%, 70%, 75%, 80% or 85% more preferably at least 90%, and most preferably at least 95%. Polypeptides which are "substantially similar" share sequences as noted above except that residue positions which are not identical may differ by conservative amino acid changes. Conservative amino acid substitutions refer to the interchangeability of residues having similar side chains. For example, a group of amino acids having aliphatic side chains is glycine, alanine, valine, leucine, and isoleucine; a group of amino acids having aliphatic-hydroxyl side chains is serine and threonine; a group of amino acids having amide-containing side chains is asparagine and glutamine; a group of amino acids having aromatic side chains is phenylalanine, tyrosine, and tryptophan; a group of amino acids having basic side chains is lysine, arginine, and histidine; and a group of amino acids having sulfur-containing side chains is cysteine and methionine. Preferred conservative amino acids substitution groups are: valine-leucine-isoleucine, phenylalanine-tyrosine, lysine-arginine, alanine-valine, and asparagine-glutamine.

Another indication that nucleotide sequences are substantially identical is if two molecules hybridize to each other, or a third nucleic acid, under stringent conditions.

More particularly, the polynucleic acids as used herein will comprise at least part of a DNA sequence which is essentially similar, or, preferentially, essentially identical or identical to one or both of the nucleotide or amino acid sequences corresponding to SEQ ID NO 1 to 121 disclosed herein, more specifically in the nucleotide sequence encoding, or the amino-acid sequence corresponding to the "active domain" of the respective protein or polypeptide.

The polynucleic acid sequences according to the present invention can be produced by means of any nucleic acid amplification technique known in the art such as PCR or conventional chemical synthesis.

For a general overview of PCR see PCR Protocols (Innis et al. (1990)).

Polynucleotides may also be synthesized by well-known techniques as described in the technical literature. See, e.g., Carruthers et al. (1982) and Adams et al. (1983). Double stranded DNA fragments may then be obtained either by synthesizing the complementary strand and annealing the strands together under appropriate conditions, or by adding the complementary strand using DNA polymerase with an appropriate primer sequence.

The present invention more particularly relates to an isolated polypeptide encoded by a polynucleic acid according to any of the polynucleic acids as defined above, or a functional fragment thereof.

The present invention preferably relates to an isolated polypeptide as listed in Table 1 or to an isolated polypeptide encoded by a polynucleic acid isolated as defined above. Preferably, the present invention relates to polypeptides or peptides having at least part of the sequence of any of SEQ ID NO NO 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, or 120. Preferably, said part is a unique part and preferably includes the active domain of said polypeptide. Preferably said polypeptide is a recombinant polypeptide.

The term "isolated" distinguishes the protein or polynucleic acid according to the invention from the naturally occurring one.

The present invention also relates to a polypeptide comprising at least part of a polypeptide which is at least 50%, 55%, 60%, 65% identical, preferentially at least 70%, 75% identical, more preferably at least 80% or 85% identical, and most

preferably at least 90% or 95% identical to any of SEQ ID NO NO 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, or 120.

5 The terms "polypeptide" and "protein" are used interchangeably throughout the present description.

Said polypeptide preferably has the ability to confer tolerance or resistance to environmental stress conditions in at least plants, plant parts, plant tissues, plant cells, plant calli or yeast.

10 The term "functional fragment" refers to a fragment having substantially the biological activity of the protein from which it is derived.

15 The polypeptides of the present invention may be produced by recombinant expression in prokaryotic and eukaryotic engineered cells such as bacteria, yeast or fungi. It is expected that those of skill in the art are knowledgeable in the numerous expression systems available for expression in these systems.

20 The present invention more particularly relates to a method for producing a plant with enhanced environmental stress resistance or tolerance, said method comprising transiently introducing into a plant cell a recombinant DNA comprising any of the polynucleic acids as defined above which when (over)expressed in a plant cell enhances tolerance or resistance to environmental stress of said plant.

25 The term "plant cell" as defined above also comprises plant tissue or a plant as a whole. The present invention more particularly relates to a method for producing a plant with enhanced environmental stress resistance or tolerance, said method comprising transiently introducing into a plant cell a recombinant DNA comprising any of the polynucleic acids encoding a protein as listed in Table 1 which when (over)expressed in a plant cell enhances tolerance or resistance to environmental stress in said plant.

30 The term "(over)expression" refers to the fact that the polypeptides of the invention encoded by said polynucleic acid are preferably expressed in an amount effective to confer tolerance or resistance to the transformed plant, to an amount of salt, heat, cold, (or other stress factors) that inhibits the growth of the corresponding untransformed plant.

Several methods to obtain transient introduction and expression of a recombinant DNA in a plant are known to the art. For example, plant virus vectors can

be used to obtain such purpose. Examples conferring to the use of plant viral vectors are described in Porta and Lomonosoff (1996), WO9320217 and US 5,589,367.

The present invention also relates to a method for producing a plant with enhanced environmental stress resistance or tolerance, said method comprising stably introducing into the genome of a plant cell a recombinant DNA comprising any of the polynucleic acids as defined above which when (over)expressed in a plant cell enhances the environmental stress tolerance or resistance of a plant.

The present invention also relates to a method for producing a plant with enhanced tolerance or resistance to environmental stress conditions, said method comprising introducing into the genome of a plant cell a recombinant DNA comprising any of the polynucleic acids encoding a protein as listed Table 1 which when (over)expressed in a plant cell enhances the environmental stress resistance of said plant.

According to a preferred embodiment, the present invention relates to a method for producing a plant with enhanced tolerance or resistance to environmental stress, said method comprising introducing into said plant a polynucleic acid as defined above encoding a DBF2 kinase, preferably a plant DBF2 kinase, most preferably an *Arabidopsis* DBF2 kinase.

According to another preferred embodiment, the present invention relates to a method as defined above for producing a plant with enhanced tolerance or resistance to environmental stress, said method comprising introducing into said plant a polynucleic acid as defined above encoding an HSP 17.6A protein, preferably a plant HSP 17.6A protein, most preferably an *Arabidopsis* HSP 17.6A.

According to a preferred embodiment, the present invention relates to a method as defined above for producing a plant with enhanced tolerance or resistance to environmental stress, said method comprising introducing into said plant a polynucleic acid as defined above encoding a c74 protein, preferably a plant c74 protein, most preferably a *Arabidopsis* c74 protein.

Preferably, the present invention relates to a method as defined above, comprising:

(a) introducing into the genome of a plant cell one or more recombinant DNA molecules, said recombinant DNA molecules comprising:

- a polynucleic acid as defined above, and,
- a plant expressible promoter, whereby said polynucleic acid is in the same transcriptional unit

and under the control of said plant-expressible promoter, and,

- (b) regenerating said plant from said plant cell.

The present invention also relates to a method for producing a plant with enhanced tolerance or resistance to environmental stress, said method comprising indirectly increasing of inducing the expression of an endogenous gene in said plant comprised within a polynucleic acid as defined above or indirectly increasing of inducing the activity of a protein as defined above.

The present invention also relates to a method as defined above, comprising:

10 (a) introducing into the genome of a plant cell one or more recombinant DNA molecules, said recombinant DNA molecules comprising:

- a DNA encoding a protein which when expressed in said plant cell at an effective amount indirectly increases or induces the expression of an endogenous polynucleic acid or indirectly increases or induces the protein activity of a protein encoded by said polynucleic acid of the present invention, and,
- a plant expressible promoter, whereby said DNA is in the same transcriptional unit and under the control of said plant-expressible promoter, and,

15 20 (b) regenerating said plant from said plant cell.

A "recombinant" DNA molecule will comprise a "heterologous sequence" meaning that said recombinant DNA molecule will comprise a sequence originating from a foreign species, or, if from the same species, may be substantially modified from its original form. For example, a promoter operably linked to a structural gene which is from a species different from which the structural gene was derived, or, if from the same species, may be substantially modified from its original form.

The present invention also relates to a method as defined above for producing a plant with enhanced tolerance or resistance to environmental stress conditions, said 30 method comprising indirectly increasing or inducing the expression of an endogenous gene in said plant comprised within a polynucleic acid as defined above or indirectly increasing or inducing the activity of a protein of the invention as defined above. According to this embodiment, other polynucleic acids modulating the expression or the activity of a protein according to the present invention may be introduced

transiently or stably into the genome of said plants. The term "modulating" means enhancing, inducing, increasing, decreasing or inhibiting.

Increase or induction of expression or induction or increase of protein activity is required when said regulator protein is a positive regulator of the expression or the 5 activity of at least one of the polynucleic acids or protein of the present invention.

Decrease or inhibition of expression or decrease or inhibition of protein activity is required when said regulator protein is a negative regulator of the expression or activity of at least one of the polynucleic acids or proteins of the present invention.

Increase of the activity of said polypeptide according to the present invention is 10 obtained, according to one embodiment of the invention, by influencing endogenous gene expression in the plant. This is preferably achieved by the introduction of one or more polynucleic acid sequences according to the invention into the plant genome, in a suitable conformation for gene expression (e.g. under control of a plant-expressible promoter). This will result in increased or induced expression (overexpression) or 15 increased or induced activity of the protein in the plant cells, and, in the presence of an adequate substrate, in an increase of tolerance or resistance to environmental stress conditions in a transgenic plant or plant cell as compared to a non-transgenic plant or plant cell. This increase in tolerance can be measured by measuring mRNA levels, or where appropriate, the level or activity of the respective protein (e.g. by 20 means of ELISA, activity of the enzyme as measured by any technique known in the art). Endogenous gene expression refers to the expression of a protein which is naturally found in the plant, plant part or plant cell concerned.

Alternatively, said enhanced tolerance or resistance to environmental stress conditions may be achieved by introducing into the genome of the plant, one or more 25 transgenes which interact with the expression of endogenous genes (polynucleic acids) according to the present invention, by anti-sense RNA, co-suppression or ribozyme suppression of genes which normally inhibit the expression of the polynucleic acids of the present invention or by suppression of genes which normally inhibit the activity of the polypeptides of the invention as defined above.

For inhibition of expression, the nucleic acid segment to be introduced generally will be substantially identical to at least a portion of the endogenous gene or genes to be repressed. The sequence, however, need not be perfectly identical to inhibit expression. The vectors of the present invention can be designed such that the inhibitory effect applies to other genes within a family of genes exhibiting homology or 35 substantial homology to the target gene.

For antisense suppression, the introduced sequence also need not be full length relative to either the primary transcription product or fully processed mRNA.

Generally, higher homology can be used to compensate for the use of a shorter sequence.

5 Furthermore, the introduced sequence need not have the same intron or exon pattern, and homology of non-coding segments may be equally effective. Normally, a sequence of between about 30 or 40 nucleotides up to the full length sequence should be used, though a sequence of at least about 100 nucleotides is preferred, a sequence of at least about 200 nucleotides is more preferred, and a sequence of
10 about 500 to about 1700 nucleotides is especially preferred.

Catalytic RNA molecules or ribozymes can also be used to inhibit expression of genes as explained above. It is possible to design ribozymes that specifically pair with virtually any target RNA and cleave the phosphodiester backbone at a specific location, thereby functionally inactivating the target RNA. In carrying out this cleavage,
15 the ribozyme is not itself altered, and is thus capable of recycling and cleaving other molecules, making it a true enzyme. The inclusion of ribozyme sequences within antisense RNAs confers RNA-cleaving activity upon them, thereby increasing the activity of the constructs.

A number of classes of ribozymes have been identified. One class of
20 ribozymes is derived from a number of small circular RNAs which are capable of selfcleavage and replication in plants. The RNAs replicate either alone (viroid RNAs) or with a helper virus (satellite RNAs). Examples include RNAs from avocado sunblotch viroid and the satellite RNAs from tobacco ringspot virus, lucerne transient streak virus, velvet tobacco mottle virus, solanum nodiflorum mottle virus and
25 subterranean clover mottle virus. The design and use of target RNA-specific ribozymes is described in Haseloff et al. (1988).

Another method of suppression of gene expression is sense suppression. Introduction of nucleic acid configured in the sense orientation has been shown to be an effective means by which to block the transcription of target genes. For an example
30 of the use of this method to modulate expression of endogenous genes see, Napoli et al. (1990), and U.S. Patents Nos. 5,034,323, 5,231,020, and 5,283,184.

The suppressive effect may occur where the introduced sequence contains no coding sequence per se, but only intron or untranslated sequences homologous to sequences present in the primary transcript of the endogenous sequence. The introduced sequence generally will be substantially identical to the endogenous
35

sequence intended to be repressed. This minimal identity will typically be greater than about 65%, but a higher identity might exert a more effective repression of expression of the endogenous sequences. Substantially greater identity of more than about 80% is preferred, though about 95% to absolute identity would be most preferred. As with antisense regulation, the effect should apply to any other proteins within a similar family of genes exhibiting homology or substantial homology.

For sense suppression, the introduced sequence, needing less than absolute identity, also need not be full length, relative to either the primary transcription product or fully processed mRNA. This may be preferred to avoid concurrent production of some plants which are overexpressers. A higher identity in a shorter than full length sequence compensates for a longer, less identical sequence. Furthermore, the introduced sequence need not have the same intron or exon pattern, and identity of non-coding segments will be equally effective. Normally, a sequence of the size ranges noted above for antisense regulation is used.

Other methods for altering or replacing genes known in the art can also be used to inhibit expression of a gene. For instance, insertional mutants using T-DNA or transposons can be generated. See, e.g., Haring et al. (1991) and Walbot (1992). Another strategy in genetic engineering of plants and animals is targeted gene replacement. Homologous recombination has typically been used for this purpose (see, Capecchi (1989)).

Alternatively, the present invention also relates to a method as defined above wherein said DNA encodes a sense or antisense RNA or a ribozyme capable of indirectly increasing or inducing the expression of an endogenous polynucleic acid sequence according to the invention as defined above or increasing or inducing the activity of a protein of the invention as defined above. Preferably said endogenous polynucleic acid encodes a protein as listed in Table 1.

The present invention also relates to a recombinant polynucleic acid comprising: a polynucleic acid as defined above, and, a plant expressible promoter, whereby said polynucleic acid is in the same transcriptional unit and under the control of said plant-expressible promoter.

The present invention also relates to a recombinant polynucleic acid comprising:

(a) a DNA encoding a protein which when expressed in said plant at an effective amount indirectly increases or induces the expression of an endogenous

polynucleic acid as defined above or indirectly increases or induces the protein activity of a polypeptide as defined above, and,

(b) a plant expressible promoter, whereby said DNA is in the same transcriptional unit and under the control of said plant-expressible promoter.

5 An "endogenous" polynucleic acid refers to a polynucleic acid that is already present in the plant species before transformation.

Said recombinant polynucleic acid as described here above is generally also referred to as a "recombinant vector" or an "expression cassette". An expression cassette of the invention can be cloned into an expression vector by standard 10 methods. The expression vector can then be introduced into host cells by currently available DNA transfer methods.

The present invention also relates to the recombinant polynucleic acid as defined above, comprising a DNA which encodes an anti-sense RNA, a ribozyme or a sense RNA which increases or induces the activity of a protein as defined above in 15 said cell. Preferably said protein is listed in Table 1.

More particularly, the present invention relates to a recombinant polynucleic acid comprising at least part of the nucleotide sequence of any of SEQ ID NO 1, 3, 5, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 20 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, or 121.

Preferably, the present invention relates to a recombinant polynucleic acid comprising at least part of the coding sequence of a gene encoding a protein as listed in Table 1. Preferably, said "part" is a unique part of any of said nucleotide sequences. (26-28) As used herein, the term a "plant-expressible promoter" refers to a promoter 25 that is capable of driving transcription in a plant cell. This includes any promoter of plant origin, including the natural promoter of the transcribed DNA sequence, but also any promoter of non-plant origin which is capable of directing transcription in a plant cell. The promoter may also be an artificial or synthetic promoter. The term "plant-expressible promoter" includes, but is not restricted to, constitutive, inducible, organ-, tissue-specific or developmentally regulated promoters.

According to the invention, production and/or activity of a polypeptide according to the present invention in a plant or in plant parts is increased by introducing *one or more* polynucleic acids according to the invention into the genome of the plant. More specifically, the constitutive promoter can be, but is not restricted to, one of the 30 following: a 35S promoter (Odell et al. (1985)), a 35S'3 promoter (Hull and Howell 35

(1987)), the promoter of the nopaline synthase gene ("PNOS") of the Ti-plasmid (Herrera -Estrella, (1983)) or the promoter of the octopine synthase gene ("POCS", De Greve et al. (1982)). It is clear that other constitutive promoters can be used to obtain similar effects. A list of plant-expressible promoters that can be used according to the 5 present invention is given in Table 2.

For specific embodiments of this invention, the use of inducible promoters can provide certain advantages. Modulation of protein levels or protein activity may be required in certain parts of the plant, making it possible to limit modulation to a certain period of culture or developmental stage of the plant.

10 For specific embodiments of this invention, the use of organ- or tissue-specific or chemical inducible promoters can provide certain advantages. Thus, in specific embodiments of the invention, the gene(s) or part thereof is (are) placed under the control of a promoter directing expression in specific plant tissues or organs, such as for instance roots, leaves, harvestable parts, etc.

15 It is also possible to use a promoter that can be induced upon the environmental stress conditions. Such promoters can be taken for example from stress-related genes which are regulated directly by an environmental, i.e. preferable abiotic, stress in a plant cell, including genes for which expression is increased, reduced or otherwise altered. These stress related genes comprise genes the 20 expression of which is either induced or repressed by anaerobic stress, flooding stress, cold stress, dehydration stress, drought stress, heat stress or salinity. An exemplary list of such promoters is given in Table 3.

The recombinant polynucleic acids according to the present invention may include further regulatory or other sequences from other genes, such as leader 25 sequences (e.g. the cab22 leader from Petunia), 3' transcription termination and polyadenylation signals (e.g. from the octopine synthase gene or the nopaline synthase gene), plant translation initiation consensus sequences, introns, transcription enhancers and other regulatory elements such as adh intron 1, etc, which is or are operably linked to the gene or a fragment thereof. Additionally, the recombinant 30 polynucleic acid can be constructed and employed to target the gene product of the polynucleic acid of the invention to a specific intracellular compartment within a plant cell or to direct a protein to the extracellular environment. This can generally be obtained by operably joining a DNA sequence encoding a transit or signal peptide to the recombinant polynucleic acid.

The recombinant DNA comprising one or more polynucleic acids according to the present invention may be accompanied by a chimeric marker gene (Hansen et al., 1999 and references therein). The chimeric marker gene can comprise a marker DNA that is operably linked at its 5' end to a plant-expressible promoter, preferably a 5 constitutive promoter, such as the CaMV 35S promoter, or a light inducible promoter such as the promoter of the gene encoding the small subunit of Rubisco; and operably linked at its 3' end to suitable plant transcription 3' end formation and polyadenylation signals. It is expected that the choice of the marker DNA is not critical, and any suitable marker DNA can be used. For example, a marker DNA can encode a protein 10 that provides a distinguishable color to the transformed plant cell, such as the A1 gene (Meyer et al., (1987)), can provide herbicide resistance to the transformed plant cell, such as the *bar* gene, encoding resistance to phosphinothricin (EP 0 242 246), or can provide antibiotic resistance to the transformed cells, such as the *aac(6')* gene, encoding resistance to gentamycin (WO94/01560).

15 According to another embodiment, the present invention relates to the use of the polynucleic acids above as selectable marker gene. More preferably, the present invention also relates to the use of the plant DBF2 gene as defined above as selectable marker gene, selection taking place with treatment with a stress condition.

20 The recombinant DNA vectors according to the present invention comprising the sequences from genes of the invention will typically also comprise a marker gene which confers a selectable phenotype on plant cells. For example, the marker may encode biocide resistance, particularly antibiotic resistance, such as resistance to kanamycin, G418, bleomycin, hygromycin, or herbicide resistance, such as resistance 25 to chlorosulfuron or Basta.

The present invention also relates to a recombinant host cell transformed with an isolated polynucleic acid as defined above. Said host can be any host known in the art. Preferably said recombinant host cell is a plant cell, yeast, fungi, insect cell, etc. In order to be efficiently expressed in said host, said polynucleic acids can be combined 30 with any promoter known to function in said host system. Methods for transforming said host cells are also well known in the art.

The present invention particularly also relates to a plant cell transformed with at least one recombinant polynucleic acid as defined above.

35 The present invention also relates to a plant consisting essentially of plant cells transformed with at least one recombinant polynucleic acid as defined above.

A "transgenic plant" refers to a plant comprising a transgene in the genome of essentially all of its cells.

DNA constructs of the invention may be introduced into the genome of the desired plant host by a variety of conventional techniques (see for example Hansen et al., 1999 for review and WO 99/05902). For example, DNA constructs of the invention may be introduced into the genome of the desired plant host by using techniques such as protoplast transformation, biolistics or microprojectile bombardment or Agrobacterium mediated transformation.

Microinjection techniques are known in the art and well described in the scientific and patent literature. The introduction of DNA constructs using polyethylene glycol precipitation is described in Paszkowski et al. (1984).

Electroporation techniques are described in Fromm et al. (1985). Biolistic transformation techniques are described in Klein et al. (1987).

Alternatively, the DNA constructs may be combined with suitable T-DNA flanking regions and introduced into a conventional Agrobacterium host vector. The virulence functions of the Agrobacterium host will direct the insertion of the construct and adjacent marker into the plant cell DNA when the cell is infected by the bacteria. Agrobacterium tumefaciens-mediated transformation techniques, including disarming and use of binary vectors, are well described in the scientific literature. See, for example Horsch et al. (1984), and Fraley et al. (1983).

Transformed plant cells which are derived by any of the above transformation techniques can be cultured to regenerate a whole plant which possesses the transformed genotype and thus the desired phenotype. Such regeneration techniques rely on manipulation of certain phytohormones in a tissue culture growth medium. Plant regeneration from cultured protoplasts is described in Evans et al. (1983); and Binding (1985). Regeneration can also be obtained from plant callus, explants, organs, or parts thereof. Such regeneration techniques are described generally in Klee et al. (1987).

The polynucleic acids and polypeptides of the invention can be used to confer desired traits on a broad range of plants, including monocotyledonous or dicotyledonous plants, preferably they belong to a plant species of interest in agriculture, wood culture or horticulture, such as a crop plant, root plant, oil producing plant, wood producing plant, fruit producing plant, fodder or forage legume, companion or ornamental or horticultured plant. The plants can include species from the genera Actinidia, Apium, Allium, Ananas, Arachis, Arisaema, Asparagus, Atropa, Avena, Beta,

Brassica, Carica, Cichorium, Citrus, Citrullus, Capsicum, Cucumis, Cucurbita, Cydonia, Daucus, Diospyros, Fragaria, Glycine, Gossypium, Helianthus, Heterocallis, Hordeum, Hyoscyamus, Ipomoea, Lactuca, Linum, Lolium, Lycopersicon, Malus, Mangifera, Manihot, Majorana, Medicago, Musa, Nicotiana, Oryza, Panicum, 5 Pannisetum, Persea, Petroselinum, Phaseolus, Pisum, Pyrus, Prunus, Raphanus, Rheum, Ribes, Rubus, Saccharum, Secale, Senecio, Sinapis, Solanum, Sorghum, Spinacia, Trigonella, Triticum, Vaccinium, Vitis, Vigna, Zea, and Zingiber. Additional species are not excluded. Crops grown on cultivated lands in arid and semi-arid areas 10 in which irrigation with ground water is needed may advantageously benefit from the invention.

One of skill will recognize that after the recombinant polynucleic acid is stably incorporated in transgenic plants and confirmed to be operable, it can be introduced into other plants by sexual crossing. Any of a number of standard breeding techniques can be used, depending upon the species to be crossed. As described before, the 15 plant cells, plant tissue, in particular, transgenic plants of the invention display a certain higher or enhanced degree of tolerance (or even resistance) to environmental stress conditions compared to the corresponding wild-type plants. For the meaning of "environmental stress", see supra. In a preferred embodiment of the present invention, the transgenic plant displays increased tolerance to osmotic stress, salt stress, cold 20 and/or heat stress. An increase in tolerance to such environmental stress is understood to refer to a tolerance to a level of such stress which inhibits the growth and productivity of the corresponding untransformed plant, as determined by methodologies known to the art. Such increased tolerance in transgenic plants is related to an increased expression level in the transgenic plant or parts thereof of one 25 or more of the polynucleic acids of the present invention and/or to an increased level of activity of the polypeptide(s) encoded by said polynucleic acid, as determined by methodologies known to the art. In comparison with their untransformed counterparts, and determined according to methodologies known in the art, a transgenic plant according to the present invention shows an increased growth, viability, metabolism, 30 fertility and/or productivity under mild environmental stress conditions. In the alternative, a transgenic plant according to the invention can grow under environmental stress conditions wherein the untransformed counterparts can not grow. An increase in tolerance to salt stress is understood to refer to the capability of the transgenic plant to grow under stress conditions which inhibit the growth of at least 35 95% of the parent, non-stress tolerant plants from which the stress tolerant transgenic

plants are derived. Typically, the growth rate of stress tolerant plants of the invention will be inhibited by less than 50%, preferably less than 30%, and most preferably will have a growth rate which is not significantly inhibited by growth conditions which inhibit the growth of at least 95% of the parental, non-stress tolerant plants. In an alternative 5 example, under mild environmental stress conditions, the growth and/or productivity of the transgenic plants is statistically at least 1 % higher than for their untransformed counterparts, preferably more than 5 % higher and most preferably more than 10 % higher.

Any transformed plant obtained according to the invention can be used in a 10 conventional breeding scheme or in *in vitro* plant propagation to produce more transformed plants with the same characteristics and/or can be used to introduce the same characteristic in other varieties of the same or related species.

Furthermore, the characteristic of the transgenic plants of the present invention to maintain normal/rapid/high growth rates under environmental stress conditions can 15 be combined with various approaches to confer environmental stress tolerance with the use of other stress tolerance genes. Some examples of such stress tolerant genes are provided in Holmberg and Bülow (1998). Most prior art approaches which include the introduction of various stress tolerance genes have the drawback that they result in reduced or abnormal growth (compared to non-transgenic controls) under normal, 20 non-stressed conditions, namely stress tolerance comes at the expense of growth and productivity (Kasuga et al., 1999). This correlation between constitutive expression of stress-responsive genes and reduced growth rates under normal growth conditions indicates the presence of cross talk mechanisms between stress response control and growth control.

25 Furthermore, the characteristic of the transgenic plants of the present invention to display tolerance to environmental stress conditions can be combined with various approaches to confer to plants other stress tolerance genes, e.g., osmotic protectants such as mannitol, proline; glycine-betaine, water-channeling proteins, etc. Thus, the approach of the present invention to confer tolerance to environmental stress 30 conditions to plants can be combined with prior art approaches which include introduction of various stress tolerance genes. Combination of these approaches may have additive and/or synergistic effects in enhancing tolerance or resistance to environmental stress.

Thus, it is immediately evident to the person skilled in the art that the method of 35 the present invention can be employed to produce transgenic stress tolerant plant with

any further desired trait (see for review TIPTEC Plant Product & Crop Biotechnology 13 (1995), 312-397) comprising:

- (i) herbicide tolerance (DE-A 3701623; Stalker (1988)),
- (ii) insect resistance (Vaek (1987)),
- 5 (iii) virus resistance (Powell (1986), Pappu (1995), Lawson (1996)),
- (iv) ozone resistance (Van Camp (1994)),
- (v) improving the preserving of fruits (Oeller (1991)),
- (vi) improvement of starch composition and/or production (Stark (1992), Visser (1991)),
- 10 (vii) altering lipid composition (Voelker (1992)),
- (viii) production of (bio)polymers (Poirer (1992)),
- (ix) alteration of the flower color, e.g., by manipulating the anthocyanin and flavonoid biosynthetic pathway (Meyer (1987), WO90/12084),
- (x) resistance to bacteria, insects and fungi (Duering (1996), Strittmatter 15 (1995), Estruch (1997)),
- (xi) alteration of alkaloid and/or cardia glycoside composition,
- (xii) inducing maintaining male and/or female sterility (EP-A1 0 412 006; EP-A1 0 223 399; WO93/25695);
- (xiii) higher longevity of the inflorescences/flowers, and
- 20 (xiv) stress resistance.

Thus, the present invention relates to any plant cell, plant tissue, or plant which due to genetic engineering displays an enhanced tolerance or resistance to environmental stress obtainable in accordance with the method of the present invention and comprising a further nucleic acid molecule conferring a novel phenotype to the plant such as one of those described above.

The present invention also relates to a callus or calli consisting essentially of plant cells as defined here above. Such transgenic calli can be preferably used for the production of secondary metabolites in plant cell suspension cultures.

The present invention also relates to any other harvestable part, organ or tissue or propagation material of the plant as defined here above.

The present invention also relates to the seed of a transgenic plant as defined here above, comprising said recombinant DNA.

The present invention also relates to the use of any isolated polynucleic acid as defined above to produce transgenic plants.

The present invention also relates to the use of a recombinant polynucleic acid as defined above, to produce transgenic plants, preferably transgenic plants having an enhanced tolerance or resistance to environmental stress conditions. Preferably said polynucleic acid encodes a polypeptide as listed in Table 1.

5 The present invention also relates to the use of an isolated polynucleic acid as defined above, to produce transgenic callus having an enhanced tolerance or resistance to environmental stress conditions. Preferably said polynucleic acid encodes a polypeptide as listed in Table 1.

10 The present invention also relates to probes and primers derived from the genes of the invention that are useful for instance for the isolation of additional genes having sequences which are similar to but differ from any of SEQ ID NO 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, or 121, but which encode a protein
15 having substantially the same biological activity as a protein having the amino acids sequence of any of SEQ ID NO 2 to 120 (even numbers) by techniques known in the art, such as PCR. The presence of a homologous gene in another plant species can for instance be verified by means of Northern or Southern blotting experiments.

20 The present invention also relates to the cloning of the genomic counterpart of any of the cDNA sequences as represented in SEQ ID NO 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, or 121. These genomic counterparts can be selected from a genomic library using these cDNA sequences as a probe. The present invention also relates to the coding region as well as the promoter region of any of said genomic clones.

25 The term "probe" according to the present invention refers to a single-stranded oligonucleotide *sequence* which is designed to specifically hybridize to any of the polynucleic acids of the invention.

30 The term "primer" refers to a single stranded oligonucleotide sequence capable of acting as a point of initiation for synthesis of a primer extension product which is complementary to the nucleic acid strand to be copied. Preferably the primer is about 5-50 nucleotides long. The term "target region" of a probe or a primer according to the present invention is a sequence within the polynucleic acid(s) to which the probe or the
35 primer is completely complementary or partially complementary (i.e. with some degree

of mismatch). It is to be understood that the complement of said target sequence is also a suitable target sequence in some cases.

"Specific hybridization" of a probe to a target region of the polynucleic acid(s) means that the probe forms a duplex with part of this region or with the entire region 5 under the experimental conditions used, and that under those conditions this probe does substantially not form a duplex with other regions of the polynucleic acids present in the sample to be analysed.

"Specific hybridization" of a primer to a target region of the polynucleic acid(s) means that, during the amplification step, said primer forms a duplex with part of this 10 region or with the entire region under the experimental conditions used, and that under those conditions the primer does not form a duplex with other regions of the polynucleic acids present in the sample to be analysed. It is to be understood that "duplex" as used hereby, means a duplex that will lead to specific amplification.

Preferably, the probes of the invention are about 5 nucleotides to about 1 Kb 15 long, more preferably from about 10 to 25 nucleotides. The nucleotides as used in the present invention may be ribonucleotides, deoxyribonucleotides and modified nucleotides such as inosine or nucleotides containing modified groups which do not essentially alter their hybridization characteristics. The probes according to the present invention preferably include parts of the cDNA sequences of any of the polynucleic 20 acids as defined above.

The present invention also relates to a composition comprising a polynucleic acid sequence as defined above, a polypeptide as defined above, a probe as defined above or a primer as defined above.

The present invention also relates to a pharmaceutical or agrochemical 25 composition comprising said polynucleic acid, a polypeptide of the invention as defined above.

The present invention also relates to antibodies specifically reacting with a protein or polypeptide according to the present invention.

The following Examples describe by way of example the tolerance and/or 30 resistance to several environmental stress conditions observed for transgenic plants and yeast overexpressing some of the polynucleic acids according to the present invention. Unless stated otherwise in the Examples, all recombinant DNA techniques are carried out according to standard protocols as described in Sambrook et al. (1989) and in volumes 1 and 2 of Ausubel et al. (1994). Standard materials and methods for plant molecular work are described in Plant Molecular Biology Labiax (1993) by R.D.D. 35

Croy, jointly published by BIOS Scientific Publications Ltd. (UK) and Blackwell Scientific Publications, UK.

These examples and figures are not to be construed as limiting to any of the embodiments of the present invention as set out above. All of the references
5 mentioned herein are incorporated by reference.

BRIEF DESCRIPTION OF THE FIGURES AND TABLES

Figure 1. *At-DBF2* encodes a functional homolog of the yeast Dbf2 (A) Comparison of the deduced amino acid sequence of *At-DBF2* with that of yeast *DBF2*.
5 Gaps were introduced to optimize the alignment. Roman numerals above the *At-DBF2* sequence indicate the protein kinase catalytic subdomains defined by Hanks et al.
(1988). (B) Complementation of *dbf2*. The *dbf2* mutant S7-4A [*MATa dbf2Δ::URA3 ura3 leu2 ade5 trp1 his7*] (Toyn and Johnston, 1994) (B1) forms swollen pairs of
10 daughter cells (dumbbells) at restrictive temperature (37° C). The defective morphology of the *dbf2* mutant can be complemented by transformation with the pYX112 centromeric plasmid (Ingenius, R&D system) containing the *At-DBF2* cDNA (B2) or *DBF2* (B3); wild type (CG378 strain, *MATa ade5 leu2 trp1 ura3*) (B4). Log phase cultures were shifted from 28°C to 37°C and photographed after 16 hours. After 16 hours, 98% of the S7-4A cells arrested with a dumbbell morphology (B1) whereas
15 6,1 and 0% of dumbbells were observed in B1, B3 and B4. Strains were kindly provided by (Dr Lindl, Max Planck Institut fur Zuchungsforschung, Köln, Germany).

Figure 2. Overexpression of *DBF2* or *At-DBF2* enhances tolerance to osmotic, salt, heat and cold stress. Yeast cells were grown in YPD and cell density
20 was adjusted to OD600 at 2. (1) DY, (2) DY transformed with pYX212 containing *DBF2*, pYX-YDBF2 , (3) DY transformed with vector alone or (4) with vector containing
At-*DBF2*, pYX-AtDBF2. Serial dilutions were made in step1:10. Ten µl of each dilution was spotted on solid YPD medium (control) supplemented with 2M sorbitol (osmotic
25 stress) or 1.2 M NaCl (salt stress) or 4µl H₂O₂ (oxidative stress) and incubated at 28° C or at 42° C (heat stress) or at 4° C (cold stress) for 3 days.

Figure 3. *DBF2* and *At-DBF2* are induced by stress. (a) Northern analysis showing the kinetics of *At-DBF2* induction in plants treated with PEG 6000 20 % and the one of *DBF2* in yeast treated with sorbitol 2M for the time indicated. (b) Northern analysis of *At-DBF2* in 10 day-old-plants grown for 5 hours in control conditions (as described in Verbruggen et al. 1993) (1), at 37° C (2), with PEG 6000 20 % (3), NaCl 1% (4), at 4° C (5) or with 0.4 mM H₂O₂ (6); and of *DBF2* in yeast cells grown for 11/2 hour in YPD (1), at 37° C (2), with sorbitol 2M (3), with NaCl 1.2 M (4), at 4° C (5) or with 0.4 mM H₂O₂ (6). Control of loading has been done with EtBr staining and is shown
35 under each Northern analysis.

(c) Western analysis of At-DBF2 in Arabidopsis. Samples are similar to those analysed in (b). Antibodies used were raised against yeast Dbf2 and kindly provided by Dr L. Leindl (Max Planck Institut fur Zuchungsforschung, Koln, Germany).

5 Figure 4. *DBF2* overexpression can suppress *hog1* osmosensitivity. The
 hog1 mutant (4) [W303-1A, *MATa*, *hog1Δ:: TRP1*] and wild type (W303) (1) were
 kindly provided by Dr Thevelein (Katholieke Universiteit Leuven, Belgium). The *hog1*
 mutant was transformed with pYX-YDBF2 (2) or pYX-AtDBF2 (3). Each of the 4
10 strains was grown for 16 hours in YPD (rich medium), and cell density was adjusted to
 OD600 at 2. Serial dilutions, 1:10 were made at five consecutive steps. Ten microliter
 of each dilution was spotted on solid YPD medium (control) or solid YPD medium
 supplemented with 0,9 M NaCl and incubated at 28°C for 3 days.

15 Figure 5. *T-DBF2* (*Nicotiana tabacum* DBF2) is periodically expressed during
 plant cell cycle. Tobacco *DBF2* expression has been followed in BY2 cells
 synchronised with aphidicolin (a & b) or with propyzamide (c & d) with *At-DBF2* as
 probe. The measure of relative rate of DNA synthesis and of the mitotic index, the use
 of the cell cycle markers *CYCB1.2* and *H4* markers have been previously described
 (Reicheld et al., 1995). *T-DBF2* transcript levels were quantified from the blots shown
20 in b and d using a PhosphorImager (Molecular Dynamics).

25 Figure 6. shows the results of a comparison of the growth of *A. thaliana* plants
 transformed with the following constructs: P35S-At-DBF2 (upper left and bottom right
 section), P35S control (upper right section) and P35S-antisense At-DBF2 (bottom left
 section) upon applying a salt stress of 200 mM NaCl overnight.

30 Figure 7 shows the results of a comparison of the growth of *A. thaliana* plants
 transformed with the following constructs: P35S-At-DBF2 (upper left and bottom right
 section), P35S control (upper right section) and P35S-antisense At-DBF2 (bottom left
 section) upon applying an osmotic stress induced by 20% PEG overnight.

Figure 8 shows the results of a comparison of the growth of *A. thaliana* plants
transformed with the following constructs: P35S-At-DBF2 (upper left and bottom right
section), P35S control (upper right section) and P35S-antisense At-DBF2 (bottom left

section) upon applying a cold stress by gradually decreasing the temperature until -7°C.

Figure 9 shows the results of a comparison of the growth of *A. thaliana* plants transformed with the following constructs: P35S-At-DBF2 (upper left and bottom right section), P35S control (upper right section) and P35S-antisense At-DBF2 (bottom left section) upon applying a heat stress of 2 hours at 48°C.

Figure 10 shows the results of a comparison of the growth of *A. thaliana* plants transformed with the following constructs: P35S-At-DBF2 (upper left and bottom right section), P35S control (upper right section) and P35S-antisense At-DBF2 (bottom left section). It can be concluded that the P35S-At-DBF2 transformed plants do not show morphological abnormalities compared to the control transgenic plants.

Figure 11 shows the results of a salt stress tolerance test with transgenic *A. thaliana* plants overexpressing HSP 17.6A (A) or c74 (B). The control plants (bottom left in A en B) is a transgenic line tranformed with pBIN-35S-CaMVter. The other sections in A are 5 independently obtained transgenic lines overexpressing HSP17.6A. The other sections in B are 5 independently obtained transgenic lines overexpressing c74.

Figure 12 shows the influence of *At-DBF2* expression in sense and antisense orientations on stress tolerance. BY2 cells were transformed by *A. tumefaciens* with recombinant T-DNA vectors containing *At-DBF2* driven by CaMV 35S RNA promoter, pBIN-35S-At-DBF2 (upper left and right sections in A or diamonds in B), the CaMV 35S promoter and terminator pBIN-35S-CaMVter (bottom left sections in A or triangles in B), or antisense *At-DBF2* under the control of the CaMV 35S promoter pBIN-35S-ASAt-DBF2 (bottom right sections in A or circles in B). (A) Picture of the same amounts of transgenic cells after 3 weeks of growth on solid medium supplemented with 300 mM NaCl, 25% PEG, 2mM H₂O₂, or at 47°C (heat). (B) Growth of suspension cells in liquid medium. Upon stress, growth was measured as fresh weight and expressed as a percentage of unstressed growth (control) (a). Stresses were applied after subculturing (= day 0) at indicated temperatures (e) and concentrations of NaCl (b) PEG (c), and H₂O₂ (f). For the cold shock (d), cells were maintained at 0°C for 2 days before the 2-week culture at 22°C. For each construction data of three

independent transgenic lines were pooled. To not overload the figure, SDs are not shown (maximum 15% of measured values). (C) Northern analysis of At-DBF2+TDBF2, kin1, and HSP17.6. Total RNAs were extracted from independent lines transformed with pBIN-35S-At-DBF2 (1) and (2), pBIN-35S-CaMter (3), and pBIN-35S-ASAT-DBF2 (4). Osmotic stress was induced with 10% PEG treatment for 5 hr (stressed).

Figure 13 shows the results of the growth of *A. thaliana* plants transformed with p35S-AtHSP17.6A and P35S control (upper right section) upon applying an osmotic stress induced by 20% PEG overnight. The results of two independent experiments are shown, each performed with 3 independently obtained transgenic lines overexpressing At-HSP17.6A (upper left and bottom left and right).

Figure 14 shows the results of the germination of *A. thaliana* plants transformed with p35S-Atc74 and P35S control (bottom section) on mineral medium supplemented with 125 mM NaCl. The results of two independent experiments are shown, each performed with 2 independently obtained transgenic lines overexpressing Atc74 (2 upper sections).

20

Table 1. Classification of the *Arabidopsis thaliana* clones isolated in Example 2. Clones isolated according to the description in example 2 have been analyzed on their potential to confer tolerance. According to the method described in example 2, the tolerance of different yeast transformants expressing an *Arabidopsis* cDNA to osmotic stress and salt stress was compared with the tolerance of DY wild type cells.

- + : similar growth to the DY wild type cells;
++ : growth of the transformant is visible at a 10-fold higher dilution (1:10) than control (1:1);
+++ : growth of the transformant is visible at a 100-fold higher dilution (1:100) than control (1:1);
++++ : growth of the transformant is visible at a 1000-fold higher dilution (1:1000) than control (1:1).

Table 2. Exemplary plant-expressible promoters for use in the performance of the present invention.

Table 3. Exemplary stress-inducible promoters for use in the performance of the present invention.

EXAMPLES**Example 1. Construction of the cDNA library.**

Total RNA has been isolated from green siliques from *Arabidopsis thaliana* by
5 grinding 1 g of siliques in 4 ml extraction buffer (100 mM tris-HCl, pH 8, 10 mM EDTA,
100 mM LiCl) at 4° C, followed by phenolisation and chloroform: isoamylalcohol (24:1)
extraction. To the aqueous phase, LiCl was added up to a final concentration of 2M,
and the total RNA was allowed to precipitate overnight at 4°C. After centrifugation, the
pellet was redissolved in 400 µl H₂O and reprecipitated with ethanol. Poly(A)
10 messenger RNA was isolated from the total RNA by binding it to an oligo-dT cellulose
spun column (Pharmacia), washing the column three times with 10 mM Tris-HCl, pH
7.5, 1 mM EDTA , 0.5 M NaCl and eluting the mRNA with 10 mM Tris-HCl, pH 7.5, 1
mM EDTA at 65° C.

The eluate was precipitated with ethanol, and cDNA was synthesized using
15 MMLV- reverse transcriptase (Pharmacia) and a d(T)₁₄-Xhol primer for the first strand
and *E. coli* DNA polymerase I (Pharmacia) for the second strand.

Example 2. Yeast transformation and selection for osmotolerance.

The cDNA was cloned into pYX vectors (Ingenius, R&D systems; 2 µ based
20 pYX 212 for bank 1, ARS/CEN based pYX112 for bank 2) as EcoRI - Xhol fragments,
using an Eco RI/Not I adaptor.

In these constructs, the cDNA is under the control of the strong constitutive TPI
promoter. The yeast strain DY (MAT_a, *his3*, *can1-100*, *ade2*, *leu2*, *trp1*,
ura3::3xSV40AP1-lacZ; kindly provided by N. Jones, Imperial Cancer Research Fund,
25 London, UK) has been transformed with these cDNA libraries, using the Lithium
Acetate transformation procedure (Gietz and Schietl, 1995). After transformation with
the Arabidopsis cDNA bank, transformants have been selected for the ability to grow
in the presence of 100mM LiCl in a stepwise selection (Lee et al., 1999). LiCl is
commonly used for salt tolerance screening in yeast (Haro et al. 1991). Several *A.
thaliana* genes, conferring osmotolerance to the yeast, have been isolated (Table 1).
To further analyse the potential of the selected Arabidopsis cDNA's to confer tolerance
30 to environmental stress in yeast, each yeast transformant expressing such selected
Arabidopsis cDNA's has been exposed to osmotic stress and salt stress. Each of the
transformants was therefore grown for 16 hours in YPD (rich medium), and cell density
35 was adjusted to OD₆₀₀ at 2. Serial dilutions, 1:10, were made at three consecutive

steps. Ten microliters of each dilution was spotted on solid YPD medium (control) supplemented with 2 M sorbitol (osmotic stress) or 1.2 M NaCl (salt stress) and incubated at 28°C for 3 days. The results of this drop growth test (see also Lee et al., 1999) are shown in Table 1.

5

Example 3. Characterization of *At-DBF2*.

At-DBF2, a 1.8 kb cDNA (SEQ ID NO 1) has been identified in this screening that encodes a predicted 60.2 kDa protein showing 81 % similarity with the yeast Dbf2 transcriptional regulator. Homology (less than 40% similarity) has also been found with the putative Dbf2 homologues in human, *C. elegans* and *Drosophila* (named Ndr for nuclear Dbf2 related, Millward et al. 1995). The At-DBF2 deduced protein sequence (SEQ ID NO 2) contains the 11 domains of protein kinases (Figure 1A). Amino acids lying between the invariant residues D and N of domain VI do not match the features of serine/threonine specificity (LKPE) defined by Hanks et al. (1988) but the GSPDYIALE peptide in domain VIII does well indicate serine/threonine specificity and At-DBF2 can complement the yeast *dbf2* mutant (Figure 1B).

In mature *Arabidopsis* plants, At-DBF2 is expressed in all tested organs. The highest abundance of transcripts has been found in siliques. A Southern analysis in *Arabidopsis*, tobacco and tomato has revealed that DBF2 seems to be conserved in plants (see Example 13 below). As At-DBF2 has been identified in a screening for LiCl tolerance, its effect in other stress situations has been tested in yeast (Figure 2).

Example 4. Overexpression of *Arabidopsis* and *Saccharomyces cerevisiae* DBF2 enhances cold, heat, salt and drought tolerance in yeast.

In order to test whether the effect was specific to the plant gene, the yeast DBF2 gene has been overexpressed in the same vector. Upon a drop growth test (Figure 2 and Lee et al., 1999). A remarkable enhancement of stress tolerance can be seen at 42°C, during osmotic stress (sorbitol), and after salt and cold treatments in yeast. There is no difference between stress tolerance afforded by the plant or the yeast gene. The enhancement of stress tolerance due to the overexpression of At-DBF2 or DBF2 reflects a role for these genes in stress situations. Therefore yeast and *Arabidopsis* plants have been exposed to sorbitol- and PEG-induced osmotic stress. At-DBF2 as well as DBF2 is induced rapidly (1 to 2 hours) and transiently upon osmotic stress (Figure 3A). The expression of At-DBF2 and DBF2 has been analyzed during other environmental stresses in *Arabidopsis* plants or in yeast cells after the

time corresponding to the highest induction seen in Fig. 3A (Figure 3B). In plant as in yeast, there is a clear induction after heat, salt, osmotic and to a lesser extent after cold, which perfectly correlates with stresses to which the overexpression enhances tolerance. However, many genes are induced upon stress without relevant adaptive 5 role, amongst others because post-transcriptional mechanisms inhibit subsequent translation. Here *At-DBF2* protein amount, as detected by anti-Dbf2 antibodies, clearly increased upon stress (Figure 3C).

10 **Example 5. Both *At-DBF2* and *DBF2* can functionally complement the *hog1* mutation.**

To investigate a possible interaction between stress signaling pathways and *DBF2*, the salt sensitive *hog1* mutant was transformed with *At-DBF2* and *DBF2*. The *HOG1* MAP kinase pathway regulates osmotic induction of transcription in yeast (Schuller *et al.* 1994). The osmosensitivity of the mutant could be recovered by the 15 overexpression of both *DBF2* and *At-DBF2* (Figure 4).

Example 6. *At-DBF2* is cell cycle regulated.

DBF2 expression is cell cycle regulated where it plays a role in DNA synthesis initiation but also in nuclear division through its association with the CCR4 20 complex (Komarnitsky *et al.* 1998, Johnston *et al.* 1990). This regulation was investigated in plants. A tobacco BY-2 cell line in which the highest level of culture synchronization, compared with other plant cell lines has been achieved so far (Shaul *et al.* 1996, Reicheld *et al.* 1995) was used. Stationary phase cells were diluted into 25 fresh medium and treated with aphidicolin (blocking cells in the beginning of the S phase) for 24 hours, then washed. The percentage of synchronous mitosis after release from the aphidicolin block was about 65 % (Figure 5A-B). A 1.6-Kb tobacco *DBF2* homologue (*T-DBF2*) could be detected on Northern blot with the *At-DBF2* as a probe. *T-DBF2* steady-state transcript level clearly oscillates during the cell cycle and 30 is mainly present during S, decreases during G2 until late M from where it increases until a peak in S phase. *T-DBF2* expression occurs clearly before *CYCB1.2* (a marker of G2-M phases), but parallels the one of H4 (a S phase marker) except at the S/G2 transition, where *T-DBF2* transcripts decline earlier, and at the M/G1 transition, where *T-DBF2* expression increases earlier. The use of the cell cycle markers *CYCB1.2* and H4 is described in Reicheld *et al.*

To follow unperturbed G1 and S phases, BY2 cell suspension was synchronized using a double blocking procedure (Nagata *et al.*, 1992). After the release from the aphidicoline block, cells are treated for 4 hours with propyzamide in the beginning of the preprophase. The percentage of synchronous mitosis after the 5 release from the propyzamide block was higher than 75%. *T-DBF2* was periodically expressed with an undetectable expression until late M, a sharp increase in G1 and a peak in mid S (Figure 5C-D) which confirms results of Figures 5A-B. However a function for the plant *DBF2* in cell cycle can only be assigned with measurement of the kinase activity. In yeast, *DBF2* transcript levels do not correlate with kinase activation 10 which occurs by dephosphorylation (Toyn and Johnson, 1994). The precise function of *Dbf2* in regulation of the cell cycle is not known. An essential role has been proposed during anaphase or telophase. No activity has been measured in G1 despite evidence for a role for *Dbf2* in initiation of DNA synthesis.

As other proteins recently identified, *Dbf2* controls the M/G1 transition 15 which is a major cell cycle transition in yeast (Aerne *et al.* 1998). The existence of a M/G1 control checkpoint has been suggested in plant cells (Hemmerlin and Bach 1998) but its importance compared to G1/S and G2/M has not been investigated.

Overexpression of *DBF2* in yeast results in kinase activity throughout the cell cycle, which may be due to the saturation of a post-translational deactivating 20 mechanism (Toyn and Johnston, 1994). Overexpression of the functionnally conserved *At-DBF2* has most probably the same effect. However, the presence of *Dbf2* kinase activity at the wrong time in the cell cycle does apparently not affect its progression. In marked contrast constitutive activity has a marked effect on stress tolerance. The role played by *At-DBF2* or *DBF2* in stress is most probably independent from the cell 25 division cycle. *At-DBF2* expression is present in all plant organs (abundant expression is observed in stems where only 1-2 % cells have a mitotic activity) and can be rapidly induced upon stress. However, a link with the cell cycle is not excluded. Higher stress tolerance in yeast overexpressing *DBF2* or *At-DBF2* may be correlated to the overproduction of the kinase in G1 where yeast cells are particularly sensitive to 30 stress. Most plant cells are also thought to be blocked in G1 but the relationship with stress response is poorly known.

Example 7. Tobacco cell transformation and recombinant T-DNA Vector construction

BY2 cells were stably transformed as described (Shaul et al., 1996) by *Agrobacterium tumefaciens* C58C1Rif^R (pGV2260) strain (Deblaere et al., 1985) carrying pBIN-35S-At-DBF2 or pBIN-35S-ASAt-DBF2 recombinant binary vectors. 5 pBIN-35S-At-DBF2 is the plant binary vector pBIN m-gfp4 in which the BamHI-Sacl fragment containing the gfp reporter gene was replaced with a BamHI-Sacl fragment containing the At-DBF2 cDNA from pYX-At-DBF2. p-Bin-35S-CaMVter is the plant binary vector pBIN19 in the HindIII-Sacl restriction sites of which the hindIII-Sacl 10 fragment of pDH51 containing the cauliflower mosaic virus (CaMV) 35S RNA promoter and terminator was cloned. pBIN-35S-ASAt-DBF2 is the pBIN-35S-CaMVter vector in which the At-DBF2 cDNA was cloned in the antisense orientation from pYXAt-DBF2 in the BamHI-SmaI restriction sites, between the CaMV 35S RNA promoter and terminator. More details are described in Lee et al. (1999).

15

Example 8. Overexpression of At-DBF2 sense and antisense RNA in plant cells

20 Transgenic plant cells overexpressing *At-DBF2* were generated to test the role of this protein in stress tolerance *in planta*. Tobacco BY2 cells were stably transformed by *A. tumefaciens* carrying the *At-DBF2* cDNA driven by the strong constitutive CaMV 35S RNA promoter. The antisense *At-DBF2* RNA also was overexpressed under the control of the same promoter. Control lines were obtained by transforming tobacco 25 BY2 cells with pBIN-35S-CaMVter. Three independently obtained *At-DBF2*-overexpressing tobacco transgenic cell lines have been selected with a high and similar *At-DBF2* expression and analysed further. Three tobacco transgenic cell lines overexpressing antisense *At-DBF2* were chosen that showed an undetectable tobacco DBF2 transcript level. Both the overexpression of *At-DBF2* and the down-regulation of 30 the endogenous gene by the antisense strategy did not result in significant differences in growth after 2 weeks (Fig. 12A and 12B). On the contrary, marked differences in growth were observed after a 2-week treatment with NaCl, PEG-induced drought, cold, or high temperatures. Transgenic lines that overexpressed *At-DBF2* were clearly more tolerant than control lines. Inhibition of the endogenous DBF2 expression was 35 correlated with a higher sensitivity to those stresses. To understand the basis of stress

tolerance in *At-DBF2*-overexpressing plant cells, expression of stress-induced genes was followed in control and stress conditions (Fig. 12C). Tobacco kin1 and HSP17.6A homologues already were induced in *At-DBF2*-overexpressing tobacco cells in control conditions to a level similar to that observed during stress conditions (PEG-induced drought), suggesting that *At-DBF2* overexpression may mimic a stress signal.

Example 9. Arabidopsis transformation and recombinant T-DNA vector construction with genes conferring tolerance to environmental stress

Arabidopsis were stably transformed as described in Clarke, Wei and Lindsey
10 (1992) by Agrobacterium tumefaciens C58C1RifR (pGV2260) strains carrying pBIN-
35S-At-DBF2, pBIN-35S-At-HSP17.6A, pBIN-35S-At-c74 recombinant binary vectors.
pBIN-35S-At-DBF2 is described in Lee et al. 1999. pBIN-35S-At-HSP17.6A
recombinant binary vector was constructed as following: the EcoRI-Xhol fragment
15 containing At-HSP17.6A cDNA in pYX-HSP17.6A (recombinant pYX212) was first
cloned in pYES2 (Invitrogen) resulting in pYES-HSP17.6A. Then the BamHI-SphI
fragment of pYES-HSP17.6A containing the At-HSP17.6A cDNA was cloned in the
plant binary vector pBIN m-gfp4 in which the BamHI-SacI fragment containing the gfp
receptor gene was deleted and replaced by the At-HSP17.6A cDNA. The 3' protruding
ends generated by SacI and SphI were blunt ended by T4 DNA polymerase. pBIN-
20 35S-c74 was constructed with a similar strategy as pBIN-35S-AtHSP17.6A with an
intermediary pYES-Atc74 vector. The At-c74 cDNA was first amplified with PCR using
the primers 5' AAA AAA CAC ATA CAG GAA TTC 3' (SEQ ID NO 122) and 5' AGT
TAG CTA GCT GAG CTC GAG 3' (SEQ ID NO 123), then cloned "blunt ended" in the
vector pYES2 cut with NotI and BstXI and blunt ended with T4 DNA polymerase.
25 Subsequently, the BamHI-SphI fragment of pYES-c74 was cloned in pBINm-gfp4 as
explained supra.

Example 10. Tolerance to environmental stress in plant cells

Transgenic calli were isolated from each of the transgenic Arabidopsis lines
30 transformed with At-DBF2, At-HSP17.6A and At-c74. The growth of these transgenic
calli during salt stress was measured and compared with control calli derived from
transgenic Arabidopsis lines transformed with pBIN-35S-CaMVter. Callus pieces (25
for each transgenic line) of similar fresh weight (50 to 100 mg) were therefor grown on
callus inducing medium (Clarke et al., 1992) supplemented with 200mM NaCl. After
35 two weeks, from visual inspection, it was clear that transgenic calli transformed w.i.n

At-DBF2 or At-HSP17.6A or At-c74 looked much better than control transgenic calli transformed with pBIN-35S-CaMVter. The latter calli turned yellow and started dying. To confirm the observation, the fresh weight of the calli was measured. In comparison with the control transgenic calli, the fresh weight of the transgenic calli was for each of 5 the three lines at least five times higher than the fresh weight of the control transgenic calli.

Example 11. Tolerance to environmental stress in plants.

Seeds from transgenic Arabidopsis plants transformed with pBIN-35S-At-DBF2, 10 p-BIN-35S-At-c74, or pBIN-35S-At-HSP17.6A, were sown in bulk on nylon filters (as described in Verbruggen et al. 1993) placed on solid K1 medium supplemented with kanamycin (75 micrograms/ml). For each recombinant pBIN binary vector at least five independent transgenic lines were tested for stress tolerance. In each of these lines overexpression of the transgene has been confirmed with Northern hybridisation 15 experiments. Control plants were the ones transformed with pBIN-35S-CaMVter and transgenic plants transformed with pBIN-35S-AS+At-DBF2. After sowing, seeds were kept overnight at 4 degrees (to enhance germination). Growth was at 22 degrees, 60 % humidity, 16 hours light/8 hours dark, 70 microeinsteins. After 9 days growth, filters were transferred to liquid K1 medium supplemented with 200 mM NaCl for overnight 20 incubation. Plants were allowed to recover for 5 to 6 days by transferring the filters to solid K1 medium. Under these conditions, the control transgenic plants turned yellow, their growth was inhibited and eventually they died. On the contrary, the transgenic lines transformed with At-DBF2 or At-HSP17.6A or At-c74 survived very well (Figure 6 and Figure 11).

25 To further evaluate the scope of protection to environmental stress, transgenic plants were exposed to osmotic stress. Therefore seeds from transgenic Arabidopsis plants transformed with pBIN-35S-At-DBF2, pBIN-35S-At-c74 or pBIN-35S-At-HSP17.6A were sown in bulk on nylon filters (as described in Verbruggen et al. 1993) placed on solid K1 medium supplemented with kanamycin (75 micrograms/ml). For 30 each recombinant pBIN binary vector at least five independent transgenic lines were tested for stress tolerance. In each of these lines overexpression of the transgene has been confirmed with Northern hybridisation experiments. Control plants were the ones transformed with pBIN-35S-CaMVter and transgenic plants transformed with pBIN-35S-AS+At-DBF2. After sowing, seeds were kept overnight at 4 degrees (to enhance 35 germination). Growth was at 22 degrees, 60 % humidity, 16 hours light/8 hours dark,

70 microeinsteins. After 9 days growth, filters were transferred to liquid K1 medium supplemented with 20 % polyethylene glycol for overnight incubation. Plants were allowed to recover for 5 to 6 days by transferring the filters to solid K1 medium. Under these conditions, the control transgenic plants turned yellow, their growth was inhibited 5 and eventually they died. On the contrary, the transgenic lines transformed with At-DBF2, At-HSP17.6A or At-c74 survived very well (see Figure 7 and 13). Their growth was comparable to growth on control medium without polyethylene glycol.

To further analyse the scope of protection to environmental stress, transgenic plants were exposed to high and low temperatures. Therefor seeds from transgenic 10 plants transformed with pBIN-35S-At-DBF2 or pBIN-35S-At-c74 were sown in bulk on nylon filters (as described in Verbruggen et al. 1993) placed on solid K1 medium supplemented with kanamycin (75 micrograms/ml). For each recombinant pBIN binary vector at least five independent transgenic lines were tested for stress tolerance. In each of these lines overexpression of the transgene has been confirmed with Northern 15 hybridisation experiments. Control plants were the ones transformed with pBIN-35S-CaMVter and transgenic plants transformed with pBIN-35S-ASAt-DBF2. After sowing, seeds were kept overnight at 4 degrees (to enhance germination). Growth was at 22 degrees, 60 % humidity, 16 hours light/8 hours dark, 70 microeinsteins. After 9 days growth, for the experiments with high temperature stress, plants were exposed to 48°C 20 for two hours. For the experiments with low temperature stress, plants were exposed to gradually decreasing temperatures, down to -7°C. Plants were allowed to recover for 5 to 6 days by transferring the filters to solid K1 medium.

Under both low temperature and high temperature stress, the growth of control transgenic plants was inhibited and eventually they died. The transgenic lines 25 transformed with At-DBF2 or At-c74 survived very well. Their growth was comparable to growth under control conditions with normal temperature (see Figure 8 and 9).

To further analyse the scope of protection to environmental stress, transgenic plants were exposed to salt stress during germination. Sterilized mature seeds from transgenic plants transformed with pBIN-35S-At-DBF2 or pBIN-35S-At-c74 were 30 placed on top of petri dishes containing MS (Murashige and Skoog) medium with 0,8 % agar and 30 g l⁻¹ sucrose. Control plants were the ones transformed with pBIN-35S-CaMVter. Prior to germination and pH 5.7 adjustment, NaCl was added to a final concentration of 125 mM. Three petri dishes with a mean of 40-50 seeds per dish were used per treatment in every experiment. The complete experiment was repeated

twice. Seed germination at 22°C was followed. Seeds were considered to germinate after radical and green cotyledon emergency occurred.

On control medium (without 125 mM NaCl), germination of all transgenic lines was very similar to each other and to wild type plants. On medium supplemented with 125 mM NaCl, seeds from transgenic lines overexpressing At-DBF2 or At-c74 germinate significantly better than control transgenic lines. Less than 10 % of the seeds from transgenic lines transformed with pBIN-35S-CaMVter germinate under these conditions. In contrast, more than 70 % of the seeds from transgenic lines overexpressing At-DBF2 or At-c74 germinate on medium containing 125 mM NaCl (Figure 14).

Example 12. Southern hybridisation of At-DBF2 genes in other plants

To investigate whether *DBF2* homologues exist in other plant species, a Southern hybridisation analysis was performed using the full length *At-DBF2* as a probe. Genomic DNA was extracted from tobacco, tomato and rice according to Dellaporta et al. (1983) and further purified by phenol :chloroform extractions.

DNA (10 µg) was digested with restriction enzymes and separated on 1% (w/v) agarose gels using Lambda DNA digested with Hind III as molecular size standards. The DNA was transferred on to nylon membranes (Hybond N ; Amersham, little Chalfont, UK) in 0.4 N NaOH. Filters were UV-cross-linked for 30 seconds, prehybridized for 3 hours at 56°C in hybridization solution (2x SSPE, 0.1%(w/v) SDS, 5x Denhardt solution) using 200 gm⁻³ denatured salmon sperm DNA, and hybridized overnight with radiolabelled probes. 1X SSPE was 0.15 M NaCl/ 0.01 M sodium dihydrogen phosphate/ 1 mM EDTA

Filters were washed at 56°C in 2x SSPE, 0.1% (w/v) SDS for 20 min, then 1x SSPE, 0.1% (w/v) SDS for 20 min, and finally in 0.1x SSPE, 0.1% (w/v) SDS for 20 min. Filters were exposed to X-ray film (Kodak X-AR ; Kodak, NY, USA) in the presence of intensifying screens for 24 hours.

The results of the hybridisation experiments show that tobacco, tomato and rice have at least one homologue to At-DBF2.

Tabel 1

putative function in	Features of encoded protein	SEQ ID NO.	Growth on medium with 1,2 M NaCl	growth on medium with 2,0 M sorbitol
signalling	Similar to a yeast DBF2 cell cycle protein	1	++++	++++
metabolism	HSP17.6A	3	++++	++++
unknown	C74	5	+++	++
metabolism	Similar to ADH2	7	+	++++
metabolism	Similar to D. melanogaster catalase/catalase 3	9	++++	+
metabolism	Similar to the HSP90 heat shock protein family	11	++++	++++
metabolism	similar to phosphoenolpyruvate carboxylase	13	+	++
metabolism	pathogen related proteins, class 10	15	+	++++
metabolism	Arabidopsis ascorbate peroxidase	17	++++	++++
metabolism	similar to phosphatase binding protein	19	++++	++++
metabolism	similar to phosphatase binding protein	21	++++	++++
metabolism	similar to retinol dehydrogenase	23	+++	++++
metabolism	similar to retinol dehydrogenase	25	++++	++++
metabolism	ribosomal protein	27	++++	++++
metabolism	ribosomal protein	29	++++	++++
metabolism	similar to a protein transporter (kinase homolog)	31	++++	++++
metabolism	similar to a peptide transporter	33	++++	+
metabolism	similar to a wheat low affinity cation transporter LCT1	35	++++	++++
metabolism	similar to yeast iso-1-cytochrome c (CYC-1)	37	++++	++++
metabolism	similar to yeast OSM1	39	++++	++++
metabolism	similar to yeast copper uptake gene (CUP1)	41	++++	++
metabolism	similar to yeast UV-induced damage repair protein (RAD7)	43	++++	++++
metabolism	electron transporter, apocytochrome b	45	++++	++++
metabolism	similar to membrane lipoprotein LPPL1	47	++++	++++
metabolism	similar to tobacco auxin binding protein	49	+	++++
metabolism	similar to tobacco cytokinin binding protein CBP 57	51	++	++++
signalling	similar to calcium binding protein yeast calcineurin B	53	++	++++

signalling	similar to calcium binding protein glycine max calnexin	55	++++	+++
signalling	similar to calcium binding protein Dictyostelium discoideum calreticulin	57	++++	++++
signalling	similar to calcium binding protein calmodulin 1	59	++++	+
signalling	similar to calcium binding protein calmodulin 2	61	+	++++
signalling	MAP kinase kinase, homologous to Dicytostelium mekA (DdMek1)	63	++++	+++
signalling	similar to human adenosine kinase	65	+	++++
signalling	similar to human tyrosine kinase	67	++++	++++
signalling	similar to common ice plant tyrosine kinase	69	++++	++++
signalling	similar to the yeast protein kinase C receptor	71	++++	++++
signalling	similar to tobacco and Arabidopsis HAT7 homeotic protein	73	++	++++
signalling	similar to E. coli sigma factor regulator (RSEB)	75	+	++++
signalling	similar to human protein phosphatase 2C	77	++++	++++
metabolism	late embryogenesis abundant proteins, Arabidopsis LEA protein 10 & 14	79	++	++++
metabolism	late embryogenesis abundant proteins, Arabidopsis LEA protein 10 & 14	81	++	++++
metabolism	pathogen related proteins, class 10	83	++++	++++
metabolism	cell wall peroxidase	85	++++	+++
metabolism	ribosomal protein	87	+++	++++
metabolism	salt stress induced protein, SAS 1	89	++++	++++
metabolism	PR gene (AIG2)	91	++++	++++
metabolism	MT1c	93	++++	++++
metabolism	IPP2 (Isopentenyl diphosphate)	95	+++	++++
metabolism	chlorophyll a/b binding protein	97	+++	+++
metabolism	glutathione transferase	99	++	++++
signalling	cold- and ABA inducible, calcium dependent – kinase, Kin1	101	++++	++++
signalling	MAP kinase, Atmpk1	103	++	++++
signalling	Arabidopsis cell cycle protein histone H2A	105	++++	++++
unknown	chromosome 4 – sequence	107	+++	++++
unknown	chromosome 4 – sequence	109	+	++++
unknown	chromosome 5 – sequence	111	++++	+++
unknown	chromosome 5 – sequence	113	++++	++
unknown	chromosome 5 – sequence	115	++++	++++
unknown	chromosome 5 – sequence	117	+	++++
unknown	chromosome 5 – sequence	119	+	++++

signalling	similar to calcium binding protein centrin (caltractin)	121	++++	++++
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TABLE 2
EXEMPLARY PLANT-EXPRESSIBLE PROMOTERS FOR USE IN THE PERFORMANCE OF
THE PRESENT INVENTION

GENE SOURCE	EXPRESSION PATTERN	REFERENCE
α -amylase (<i>Amy32b</i>)	Aleurone	Lanahan <i>et al.</i> (1992); Skriver <i>et al.</i> (1991)
cathepsin β -like gene	Aleurone	Cejudo <i>et al.</i> (1992)
<i>Agrobacterium rhizogenes</i> <i>rolB</i>	Cambium	Nilsson <i>et al.</i> (1997)
PRP genes	cell wall	http://salus.medium.edu/mmg/tierney/html
barley <i>ltr1</i> promoter	Endosperm	
synthetic promoter	Endosperm	Vicente-Carabajosa <i>et al.</i> (1998)
AtPRP4	Flowers	http://salus.medium.edu/mmg/tierney/html
chalcone synthase (<i>chsA</i>)	Flowers	van der Meer <i>et al.</i> (1990)
<i>apetala-3</i>	Flowers	
Chitinase	fruit (berries, grapes, etc)	Thomas <i>et al.</i> CSIRO Plant Industry, Urrbrae, South Australia, Australia; http://winetitles.com.au/gwrdc/csh95-1.html
rbcs-3A	green tissue (eg leaf)	Lam <i>et al.</i> (1990); Tucker <i>et al.</i> (1992)
leaf-specific genes	Leaf	Baszcynski <i>et al.</i> (1988)
AtPRP4	Leaf	http://salus.medium.edu/mmg/tierney/html
<i>Pinus cab-6</i>	Leaf	Yamamoto <i>et al.</i> (1994)
SAM22	Senescent leaf	Crowell <i>et al.</i> (1992)
<i>R. japonicum</i> <i>nif</i> gene	Nodule	United States Patent No. 4, 803, 165
<i>B. japonicum</i> <i>nifH</i> gene	Nodule	United States Patent No. 5, 008, 194

GmENOD40	Nodule	Yang <i>et al.</i> (1993)
PEP carboxylase (PEPC)	Nodule	Pathirana <i>et al.</i> (1992)
Leghaemoglobin (Lb)	Nodule	Gordon <i>et al.</i> (1993)
<i>Tungro bacilliform</i> virus gene	Phloem	Bhattacharyya-Pakrasi <i>et al.</i> (1992)
sucrose-binding protein gene	plasma membrane	Grimes <i>et al.</i> (1992)
pollen-specific genes	pollen; microspore	Albani <i>et al.</i> (1990); Albani <i>et al.</i> (1991)
maize pollen-specific gene	Pollen	Hamilton <i>et al.</i> (1992)
sunflower pollen-expressed gene	Pollen	Baltz <i>et al.</i> (1992)
<i>B. napus</i> pollen-specific gene	pollen; anther; tapetum	Arnoldo <i>et al.</i> (1992)
root-expressible genes	Roots	Tingey <i>et al.</i> (1987); An <i>et al.</i> (1988);
tobacco auxin-inducible gene	root tip	Van der Zaal <i>et al.</i> (1991)
β-tubulin	Root	Oppenheimer <i>et al.</i> (1988)
Tobacco root-specific genes	Root	Conkling <i>et al.</i> (1990)
<i>B. napus</i> G1-3b gene	Root	United States Patent No. 5, 401, 836
SbPRP1	Roots	Suzuki <i>et al.</i> (1993)
AtPRP1; AtPRP3	roots; root hairs	http://salus.medium.edu/mmg/tierney/html
RD2 gene	root cortex	http://www2.cnsu.edu/ncsu/research
TobRB7 gene	root vasculature	http://www2.cnsu.edu/ncsu/research
AtPRP4	leaves; flowers; lateral root primordia	http://salus.medium.edu/mmg/tierney/html
Seed-specific genes	Seed	Simon <i>et al.</i> (1985); Scofield <i>et al.</i> (1987); Basczynski <i>et al.</i> (1990)
Brazil Nut albumin	seed	Pearson <i>et al.</i> (1992)
Legumin	Seed	Ellis <i>et al.</i> (1988)
Glutelin (rice)	Seed	Takaiwa <i>et al.</i> (1986); Takaiwa <i>et al.</i>

		(1987)
Zein	Seed	Matzke <i>et al.</i> (1990)
NapA	Seed	Stalberg <i>et al.</i> (1996)
Sunflower oleosin	seed(embryo and dry seed)	Cummins <i>et al.</i> (1992)
<i>LEAFY</i>	shoot meristem	Weigel <i>et al.</i> (1992)
<i>Arabidopsis thaliana knat1</i>	shoot meristem	Accession number AJ131822
<i>Malus domestica kn1</i>	shoot meristem	Accession number Z71981
<i>CLAVATA1</i>	shoot meristem	Accession number AF049870
Stigma-specific genes	Stigma	Nasrallah <i>et al.</i> (1988); Trick <i>et al.</i> (1990)
Class I patatin gene	Tuber	Liu <i>et al.</i> (1991)
<i>Blz2</i>	Endosperm	EP99106056.7
PCNA rice	Meristem	Kosugi <i>et al.</i> (1991); Kosugi and Ohashi (1997)

Table 3. Stress inducible promoters

Name	Stress	Reference
P5CS (delta(1)-pyrroline-5-carboxylate syntase)	salt, water	Zhang et al; Plant Science. Oct 28 1997; 129(1): 81-89
cor15a	Cold	Hajela et al., Plant Physiol. 93: 1246-1252 (1990)
cor15b	Cold	Wilhelm et al., Plant Mol Biol. 1993 Dec; 23(5):1073-7
cor15a (-305 to +78 nt)	cold, drought	Baker et al., Plant Mol Biol. 1994 Mar; 24(5): 701-13
rd29	salt, drought, cold	Kasuga et al., Nature Biotechnology, vol 18, 287-291, 1999
heat shock proteins, including artificial promoters containing the heat shock element (HSE)	Heat	Barros et al., Plant Mol Biol, 19(4): 665-75, 1992. Marrs et al., Dev Genet., 14(1): 27-41, 1993. Schoffl et al., Mol Gen Gent, 217(2-3): 246-53, 1989.
smHSP (small heat shock proteins)	heat	Waters et al, J Experimental Botany, vol 47, 296, 325-338, 1996
wcs120	Cold	Ouellet et al., FEBS Lett. 423, 324-328 (1998)
ci7	Cold	Kirch et al., Plant Mol Biol, 33(5): 897-909, 1997 Mar
Adh	cold, drought, hypoxia	Dolferus et al., Plant Physiol, 105(4): 1075-87, 1994 Aug
pws18	water: salt and drought	Joshee et al., Plant Cell Physiol, 39(1): 64-72, 1998, Jan
ci21A	Cold	Schneider et al., Plant Physiol, 113(2): 335-45, 1997
Trg-31	Drought	Chaudhary et al., Plant Mol Biol, 30(6): 1247-57, 1996
Osmotin	Osmotic	Raghothama et al., Plant Mol Biol, 23(6): 1117-28, 1993

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Porta et al. (1996), Mol Biol, 5(3):209-21

Claims

1. A method for obtaining polynucleic acids comprising coding sequences and/or genes involved in environmental stress in plants, comprising the preparation of a cDNA library comprising coding sequences from siliques, introducing said coding sequences in yeast cells in a functional format and screening for polynucleic acids leading to an enhanced tolerance or resistance to environmental stress conditions in said transformed yeast cells.
- 10 2. An isolated polynucleic acid obtainable by a method according to claim 1.
3. The isolated polynucleic acid of claim 2 which encodes a polypeptide as listed in Table 1.
- 15 4. The isolated polynucleic acid of claim 3, which is chosen from:
 - (a) any of SEQ ID NO 1, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 or 121, or the complementary strands thereof;
 - 20 (b) polynucleic acid sequences which hybridize to sequences defined in (a) or fragments thereof;
 - (c) polynucleic acid sequences which are degenerated as a result of the genetic code to the polynucleic acid sequences defined in (a) or (b); or,
 - 25 (d) polynucleic acid sequences encoding a fragment of a protein encoded by a polynucleic acid of any one of (a) to (c).
- 30 5. The isolated polynucleic acid of any of claim 2 to 4, which encodes a plant homolog of yeast DBF2 kinase.
- 35 6. The isolated polynucleic acid of claim 5, which is chosen from:
 - (a) SEQ ID NO 1, or the complementary strands thereof;
 - (b) polynucleic acid sequences which hybridize to sequences defined in (a) or fragments thereof;

- (c) polynucleic acid sequences which are degenerated as a result of the genetic code to the polynucleic acid sequences defined in (a) or (b); or,
- (d) polynucleic acid sequences encoding a fragment of a protein encoded by a polynucleic acid of any one of (a) to (c).

5

- 7. Use of an isolated polynucleic acid of claims 2 to 3 which encodes an HSP 17.6A protein for the production of transgenic plants having an enhanced tolerance or resistance to environmental stress conditions.
- 10 8. Use of an isolated polynucleic acid of claim 7 for expression of the protein encoded thereby in a plant cell, with said polynucleic acid being chosen from:
 - (a) SEQ ID NO 3, or the complementary strand thereof;
 - (b) polynucleic acid sequences which hybridize to sequences defined in (a) or fragments thereof;
 - (c) polynucleic acid sequences which are degenerated as a result of the genetic code to the polynucleic acid sequences defined in (a) or (b); or,
 - (d) polynucleic acid sequences encoding a fragment of a protein encoded by a polynucleic acid of any one of (a) to (c).
- 15 9. Use of an isolated polynucleic acid as defined above which is chosen from:
 - (a) any of SEQ ID NO 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, or 119, or the complementary strand thereof;
 - (b) polynucleic acid sequences which hybridize to sequences defined in (a) or fragments thereof;
 - (c) polynucleic acid sequences which are degenerated as a result of the genetic code to the polynucleic acid sequences defined in (a) or (b) or,
 - (d) polynucleic acid sequences encoding a fragment of a protein encoded by a polynucleic acid of any one of (a) to (c),
- 20 30 35 for the production of transgenic plants having an enhanced tolerance or resistance to environmental stress conditions.

10. The isolated polynucleic acid of any of claims 2 to 4, which encodes a c74 protein
which is chosen from:

5

- (a) SEQ ID NO 5, or the complementary strand thereof;
- (b) polynucleic acid sequences which hybridize to
sequences defined in (a) or fragments thereof;
- (c) polynucleic acid sequences which are degenerated
as a result of the genetic code to the polynucleic acid
sequences defined in (a) or (b); or,
- 10 (d) polynucleic acid sequences encoding a fragment of a
protein encoded by a polynucleic acid of any one of
(a) to (c).

10

15. An isolated polypeptide encoded by a polynucleic acid according to or as defined
in any of claims 2 to 10, or a functional fragment thereof.

20

12. The isolated polypeptide of claim 11 having at least part of the sequence of any of
SEQ ID NO 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40,
42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84,
86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, or
120.

25

13. A method for producing a plant with enhanced tolerance or resistance to
environmental stress, said method comprising transiently introducing into a plant
cell a recombinant DNA comprising a polynucleic acid of or as defined in any of
claims 2 to 10 which is expressed in an amount effective to confer enhanced
tolerance or resistance to environmental stress.

30

14. A method for producing a plant with enhanced tolerance or resistance to
environmental stress, said method comprising stably introducing into a plant cell a
recombinant DNA comprising a polynucleic acid of or as defined in any of claims 2
to 10 which is expressed in an amount effective to confer enhanced tolerance or
resistance to environmental stress.

15. The method of claims 13 or 14 for producing a plant with enhanced tolerance or resistance to environmental stress, said method comprising introducing into said plant a polynucleic acid of claims 5 or 6 encoding a plant DBF2 kinase.

5

16. The method of claim 16 for producing a plant with enhanced tolerance or resistance to environmental stress, said method comprising introducing into said plant a polynucleic acid of claims 7 or 8 encoding an HSP 17.6A protein.

10 17. The method of claim 13 to 14 for producing a plant with enhanced tolerance or resistance to environmental stress, said method comprising introducing into said plant a polynucleic acid of claim 10 encoding a c74 protein.

15 18. The method of any of claims 13 to 17, comprising introducing into the genome of a plant cell one or more recombinant DNA molecules, said recombinant DNA molecules comprising:

20

- a polynucleic acid according to or as defined in any of claims 2 to 10, and,
- a plant expressible promoter, whereby said polynucleic acid is in the same transcriptional unit and under the control of said plant-expressible promoter.

25

19. A method for producing a plant with enhanced tolerance or resistance to environmental stress, comprising introducing into the genome of a plant cell one or more recombinant DNA molecules, said recombinant DNA molecules comprising:

30

- a DNA encoding a protein which when expressed in said plant cell at an effective amount indirectly increases or induces the expression of an endogenous polynucleic acid according to or as defined in any of claims 2 to 10 or indirectly increases or induces the activity of a polypeptide of claims 11 or 12, and,

- a plant expressible promoter, whereby said DNA is in the same transcriptional unit and under the control of said plant-expressible promoter.
- 5 20. A method of claim 19 wherein said DNA encodes a sense or antisense RNA molecule or a ribozyme capable of increasing or inducing the expression of said endogenous polynucleic acid sequence according to or as defined in any of claims 2 to 10.
- 10 21. A recombinant polynucleic acid comprising:
a polynucleic acid according to or as defined in any of claims 2 to 10, and,
a plant expressible promoter, whereby said polynucleic acid is in the same transcriptional unit and under the control of said plant-expressible promoter.
- 15 22. A recombinant polynucleic acid comprising:
(a) a DNA encoding a protein which when expressed in said plant cell at an effective amount increases or induces the expression of an endogenous polynucleic acid according to or as defined in any of claims 2 to 10 or increases or induces the activity of a polypeptide of claims 11 or 12, and,
20 (b) a plant expressible promoter, whereby said DNA is in the same transcriptional unit and under the control of said plant-expressible promoter.
- 25 23. The recombinant polynucleic acid of claim 22, wherein said DNA encodes an anti-sense RNA, a ribozyme or a sense RNA which when expressed in a cell of a plant increases or induces the expression of an endogenous polynucleic acid according to or as defined in any of claims 2 to 10 or which induces or increases the activity of a protein of claim 11 or 12.
- 30 24. The recombinant polynucleic acid of claim 21 comprising at least part of the nucleotide sequence of any of SEQ ID NO 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 90, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, or 121, or part thereof.

25. The recombinant polynucleic acid of claim 21 to 24 comprising at least part of the coding sequence of a gene encoding a protein as listed in Table 1.
26. The recombinant polynucleic acid of any of claims 21 to 25 wherein said plant-expressible promoter is a constitutive promoter.
5
27. The recombinant polynucleic acid of any of claims 21 to 25 wherein said plant-expressible promoter is a stress-inducible or organ- or tissue-specific promoter.
- 10 28. The recombinant polynucleic acid of any of claims 21 to 26 wherein said plant-expressible promoter is the 35S promoter of CaMV.
29. A recombinant host cell transformed with at least one isolated polynucleic acid of or as defined in any of claims 2 to 10.
15
30. A plant cell transformed with a recombinant polynucleic acid of any one of claims 21 to 28.
31. A plant consisting essentially of plant cells of claim 30.
20
32. A callus consisting essentially of plant cells of claim 30.
33. A harvestable part, organ, tissue or propagation material of a plant of claim 31, comprising said recombinant DNA.
25
34. The use of a recombinant polynucleic acid of claim 21 to 28 to produce transgenic plants.
35. A probe which is part of the polynucleic acid sequence of or as defined in any of claims 2 to 10 and which hybridizes specifically with said polynucleic acid or the complement thereof.
30
36. A primer which is part of the polynucleic acid sequence of or as defined in any of claims 2 to 10 and which specifically amplifies said polynucleic acid or the complement thereof.
35

37. A composition comprising a polynucleic acid sequence of or as defined in any of claims 2 to 10, a polypeptide of claim 11 or 12, a probe of claim 35 or a primer of claim 36.

At-DBF2 DBF2	MAGNWSCLSTDGHGTPGGSGHFPQNLTKRRTRPAGINDSPSPVKCFFFYEDTSNTSLKEVSQPTKYSSNSPPVSPAIFYERATSCT MLSKSEKNDLLAGNMSNLSDFGNGTPGGTGLFPQNITKRRTRPAGINDSPSPVKPSFFYEDTSNMDIDEVSQPDMDVSNSPKKLPPKFYERATSNTK	89 100
I * * *		
At-DBF2 DBF2	QRVVSGRAMYFLEYCDMFDDVSSRRORTKAWLEYLQQSQLPNSDQIKLNEEWSYLOREHQVL SKRRLKPKNRDFEMITQVGOGGYGHVYLARKKDTK QRVVSCKMYFLEHYCDMFDDVSSRRORTKAWLEYLQQSQLPNSDQIKLNEEWSYLOREHQVL RKKRLKPKNRDFEMITQVGOGGYGOVYLARKKDTK	189 200
V		
At-DBF2 DBF2	EVCALKLNKKLGFKLNGTCHVLTERRSLSITSETWKLLSGTTPGGSRGHAIESELGGDFRTESIGRRCLKSGHARFYISEMFCAVNEKHLLSKT... EVCALKLNKKLFFKLNETKHLVLTERRDLTTRSEWLVKLLYAFQDQIQLSYLAMEFVPGGDFRTLINTRCLKSGHARFYISEMFCAVNALHDLGTYHDL	287 300
IV III II * *		
At-DBF2 DBF2	VII VI V * *	287 300
VIII IX * * *		
At-DBF2 DBF2	DSTISNEEDSNTIRLEKFKDLYGPAalseksIEDRKLY.....TCPNSMVGSPODYIALEVLRGKRYEYTVDYWS LKPENFLIDAKGHIKLTDFGLAACTNSERIESHKIRLEKIKOLEFFPAFTKSIEDRKHMNQLREKEINYANSMVGSPODMALEVLEGKKYDFTVDYWS	356 400
X XI *		
At-DBF2 DBF2	LGCMLFESLVGVYTPFGSSSTNETAISRSWKQTLNRARHEDGRAFYNNRTWDLJTRRADLSTRTRSFEHEVKMSYFADILFKALRSIIPPFPTPQLDSET LGCMLFESLVGVYTPFGSSSTNETDNURWKQTLRRPRQSDGRAAFSDRTADLTRLIADPINRLRSFEHVKRMSYFADINFSTLRSMIPPFPTPQLDSET	456 500
XII *		
At-DBF2 DBF2	DAGYFDDFWNEADIAKYADVFNSGCCRTALVDSAVSSKLVGFTRHRNGKGSSGMLFNGLEHSDPFSTFY DAGYFDDFTSEADMAKYADVFKRQDKLTAMVDDSAVSSKLVGFTRHRNGKGSSGILFNGLEHSDPFSTFY	528 572

FIGURE 1 A

2/15

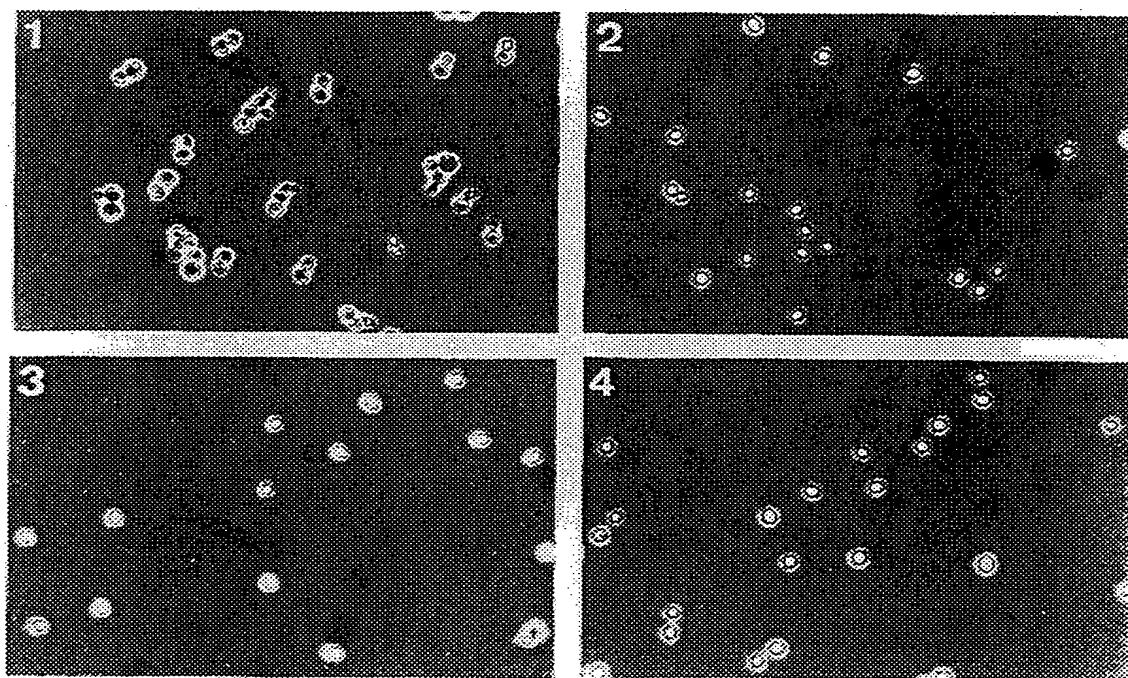


FIGURE 1B

3/15

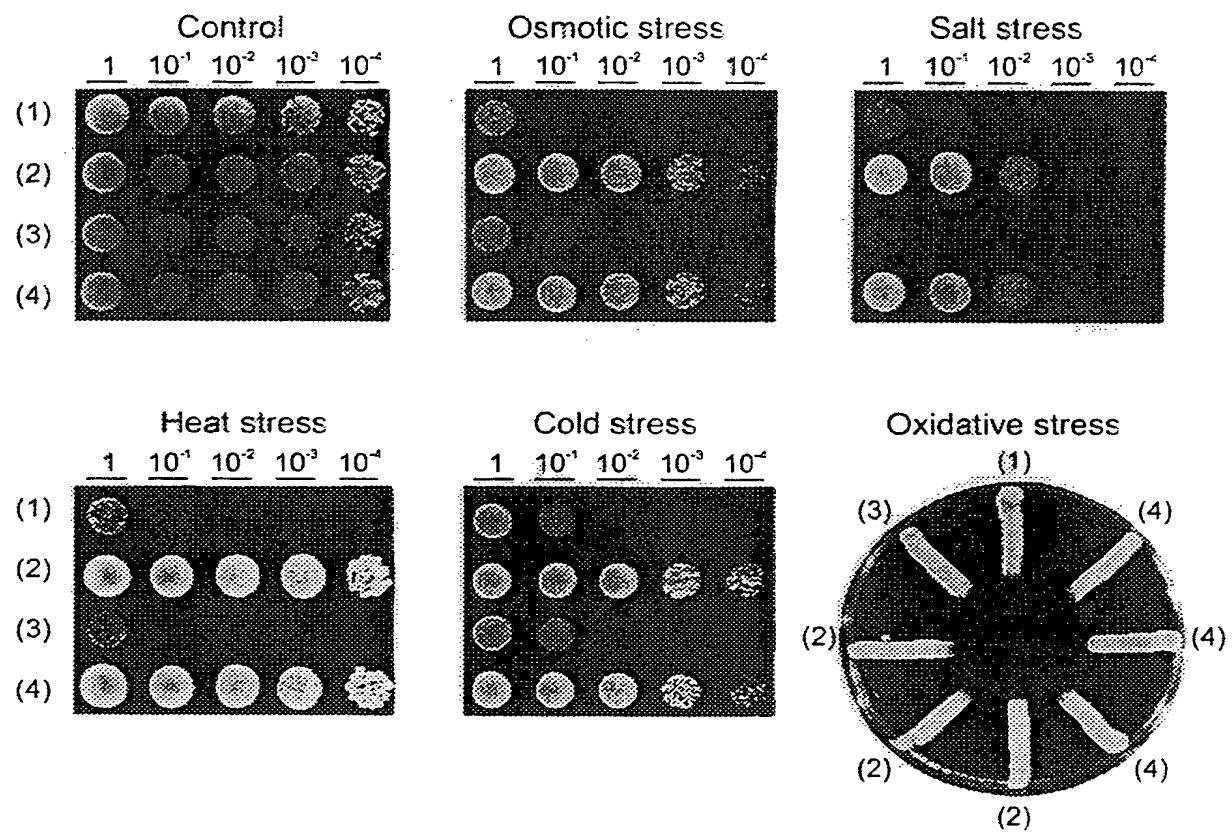


FIGURE 2

4/15

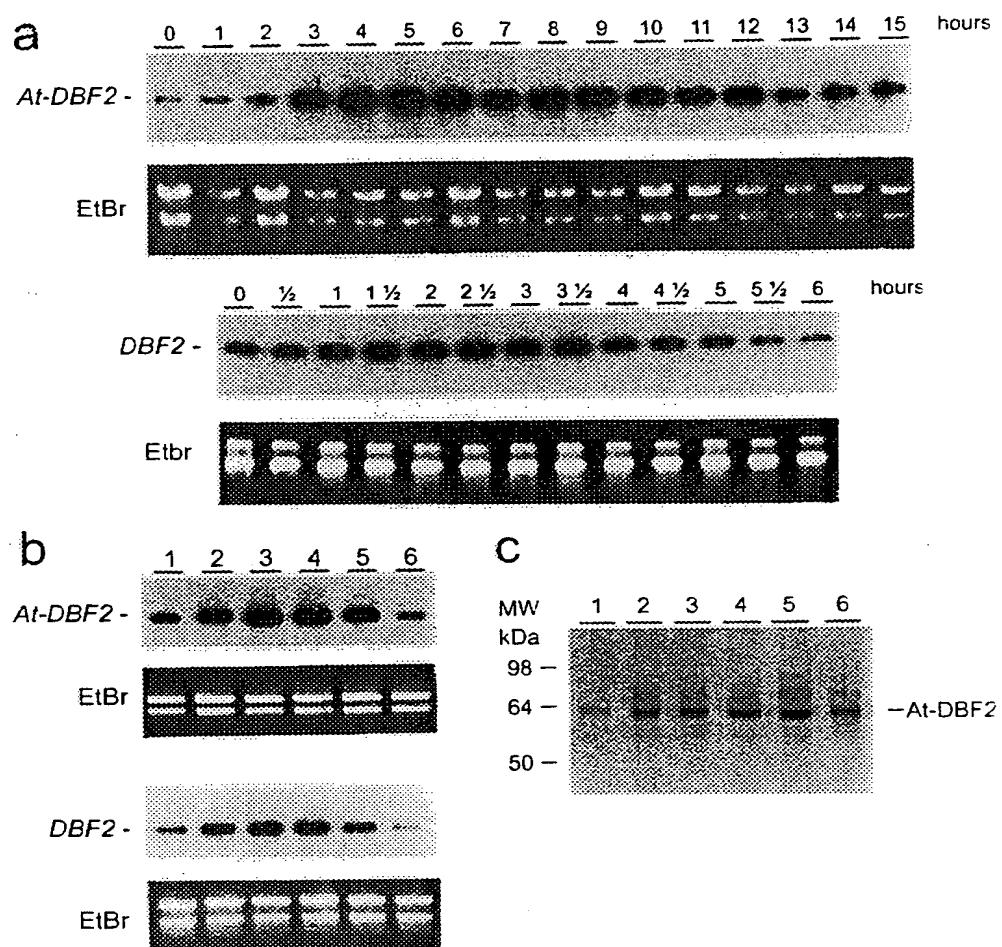


FIGURE 3

5/15

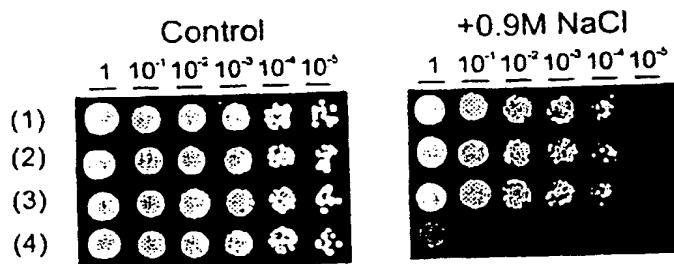


FIGURE 4

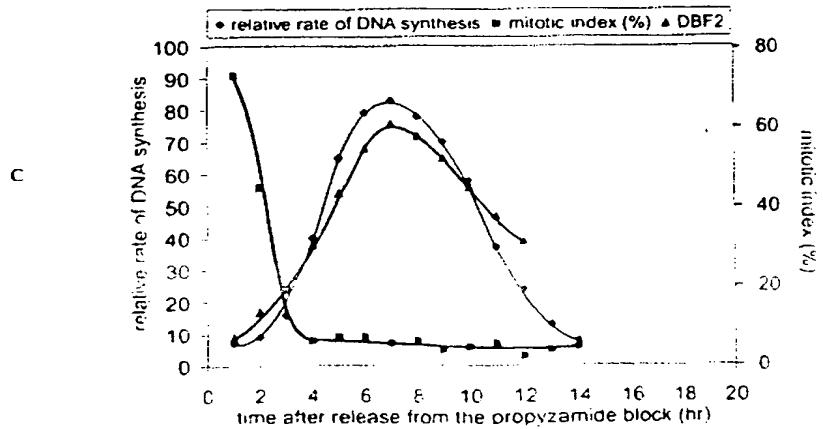
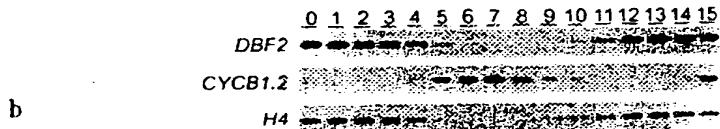
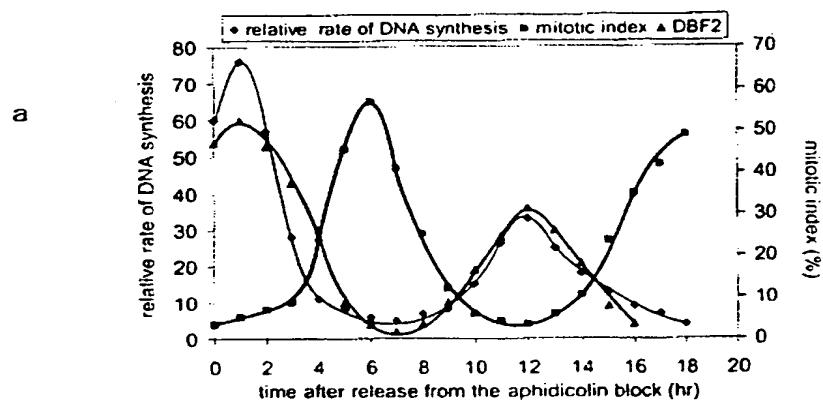


FIGURE 5

6/15

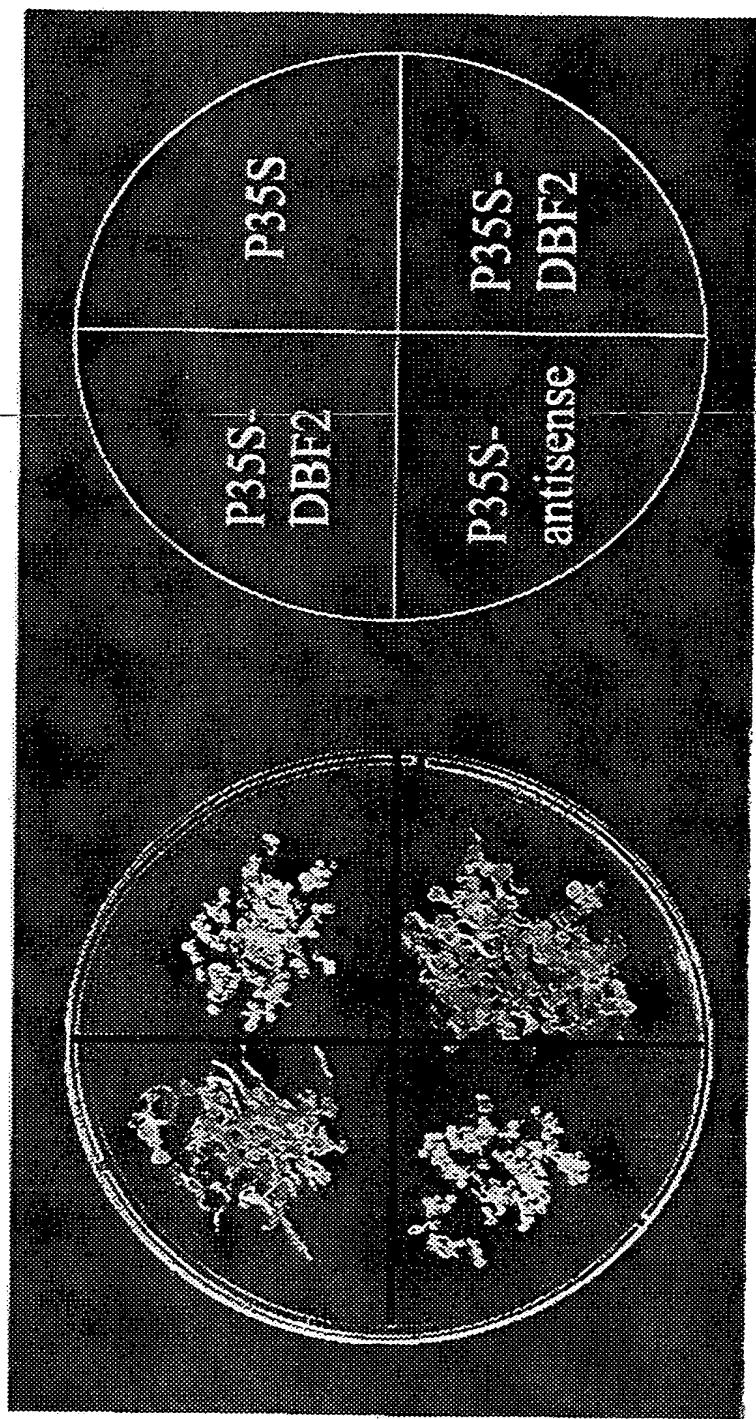


FIGURE 6

7/15

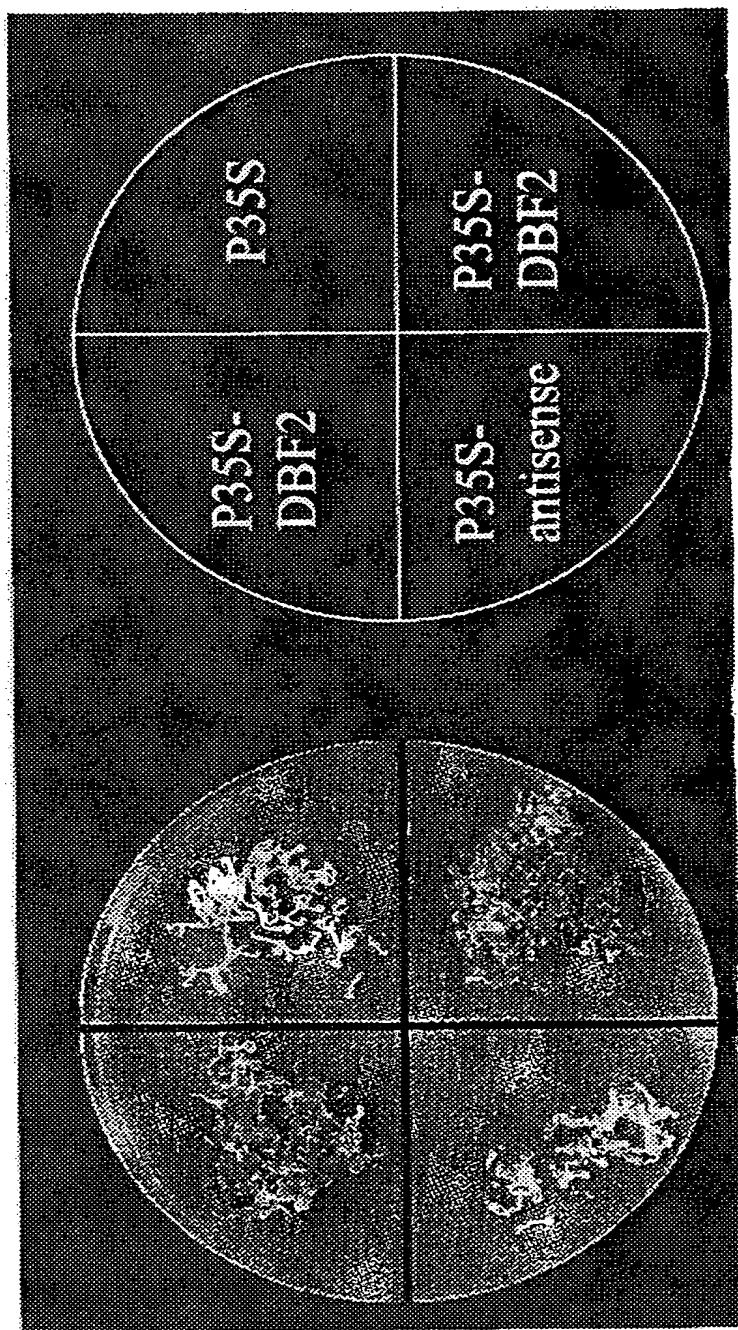


FIGURE 7

8/15

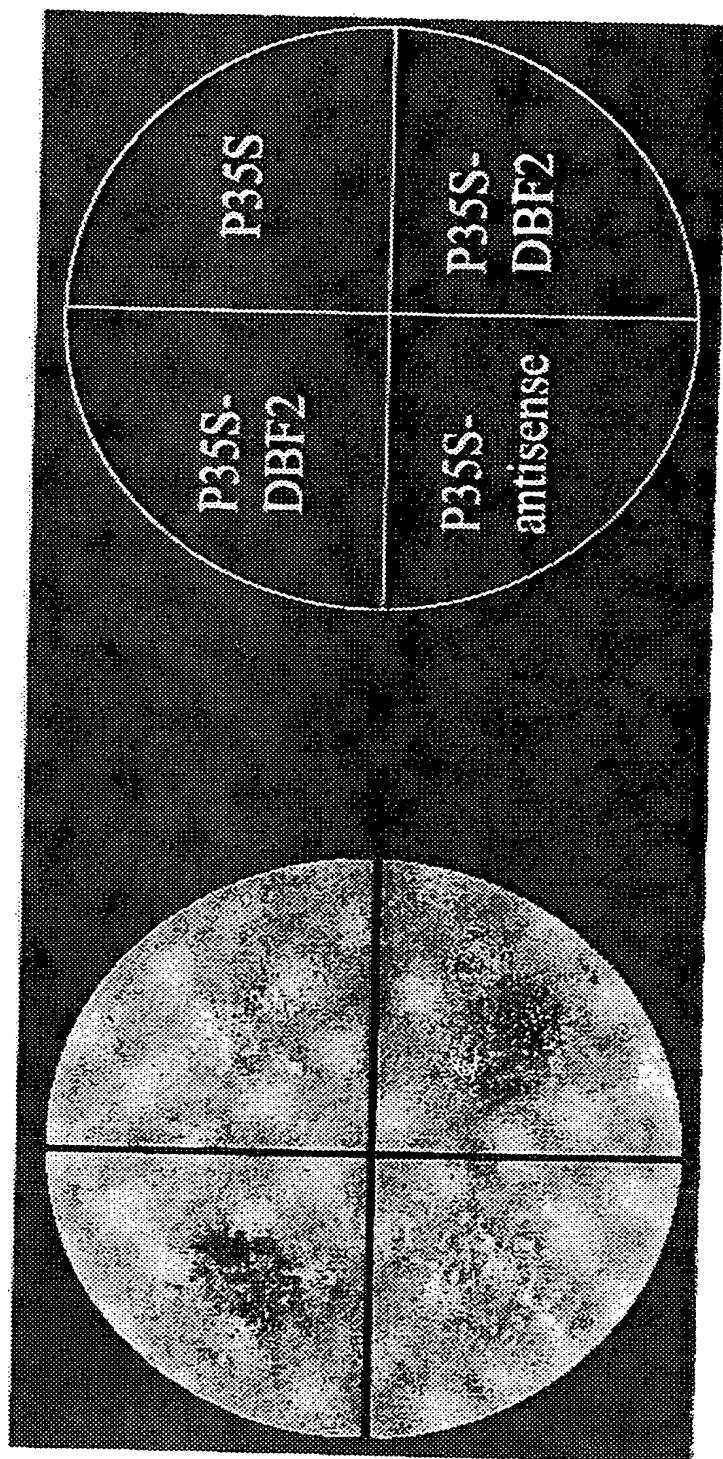


FIGURE 8

9/15

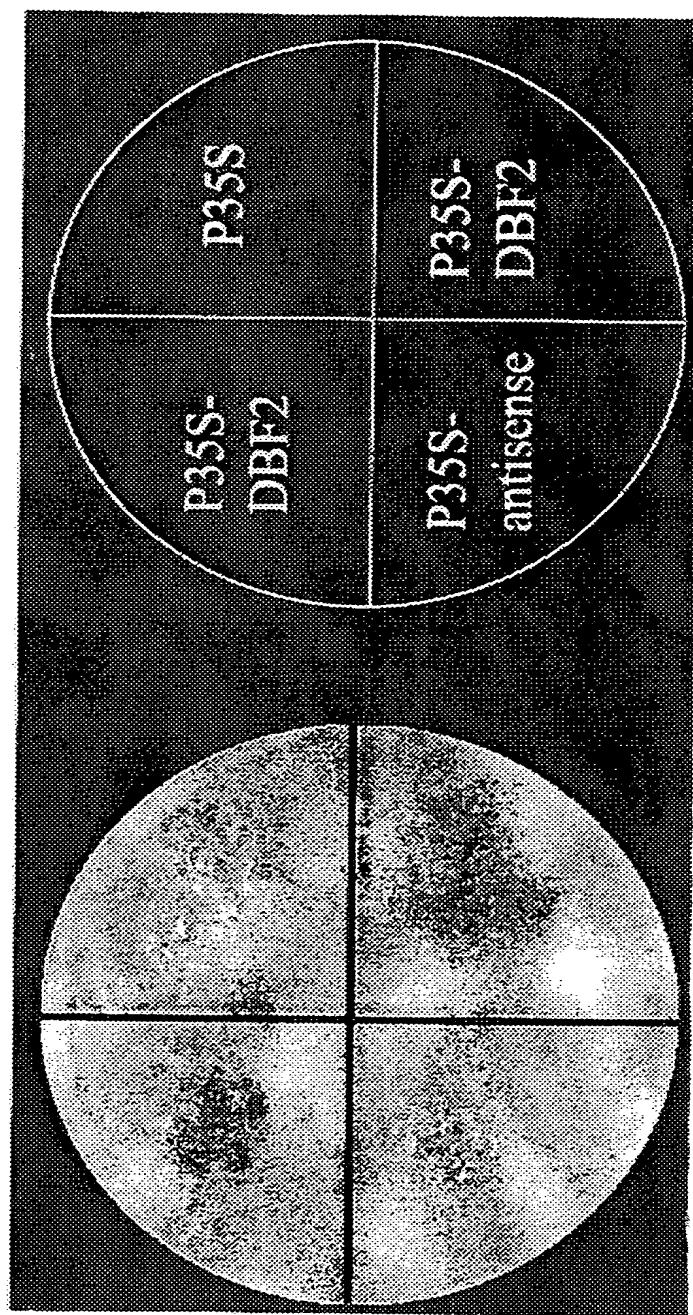


FIGURE 9

10/15

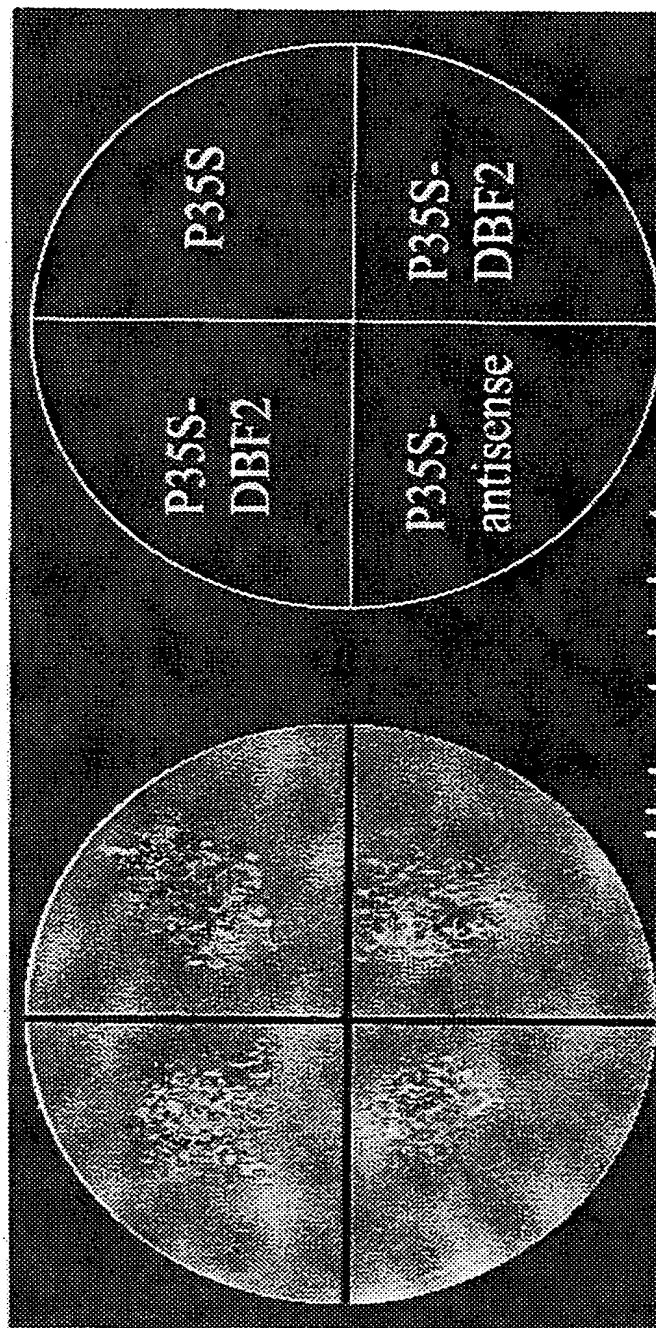


FIGURE 10

11/15

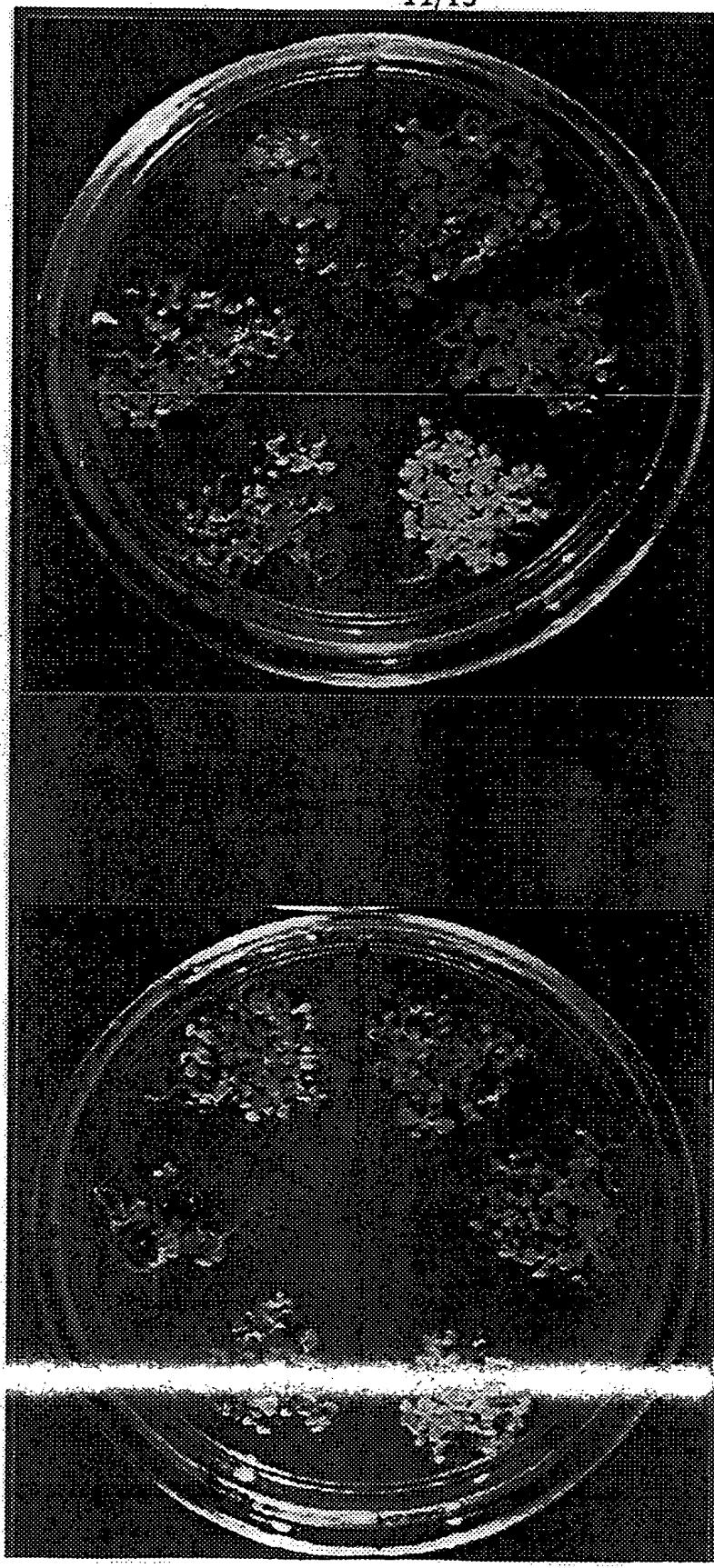


FIGURE 11

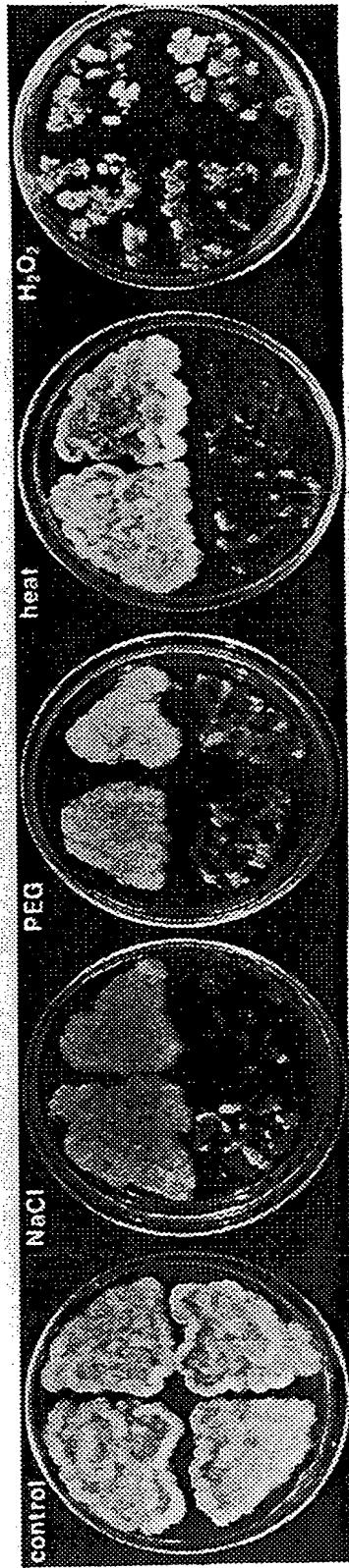


FIGURE 12A

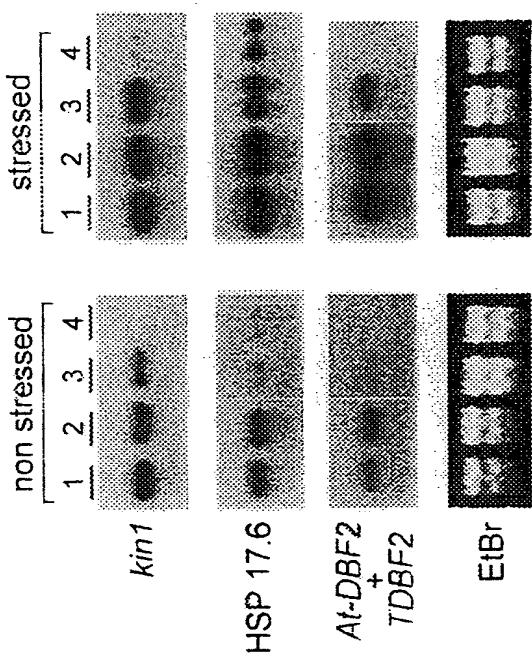


FIGURE 12C

12/15

13/15

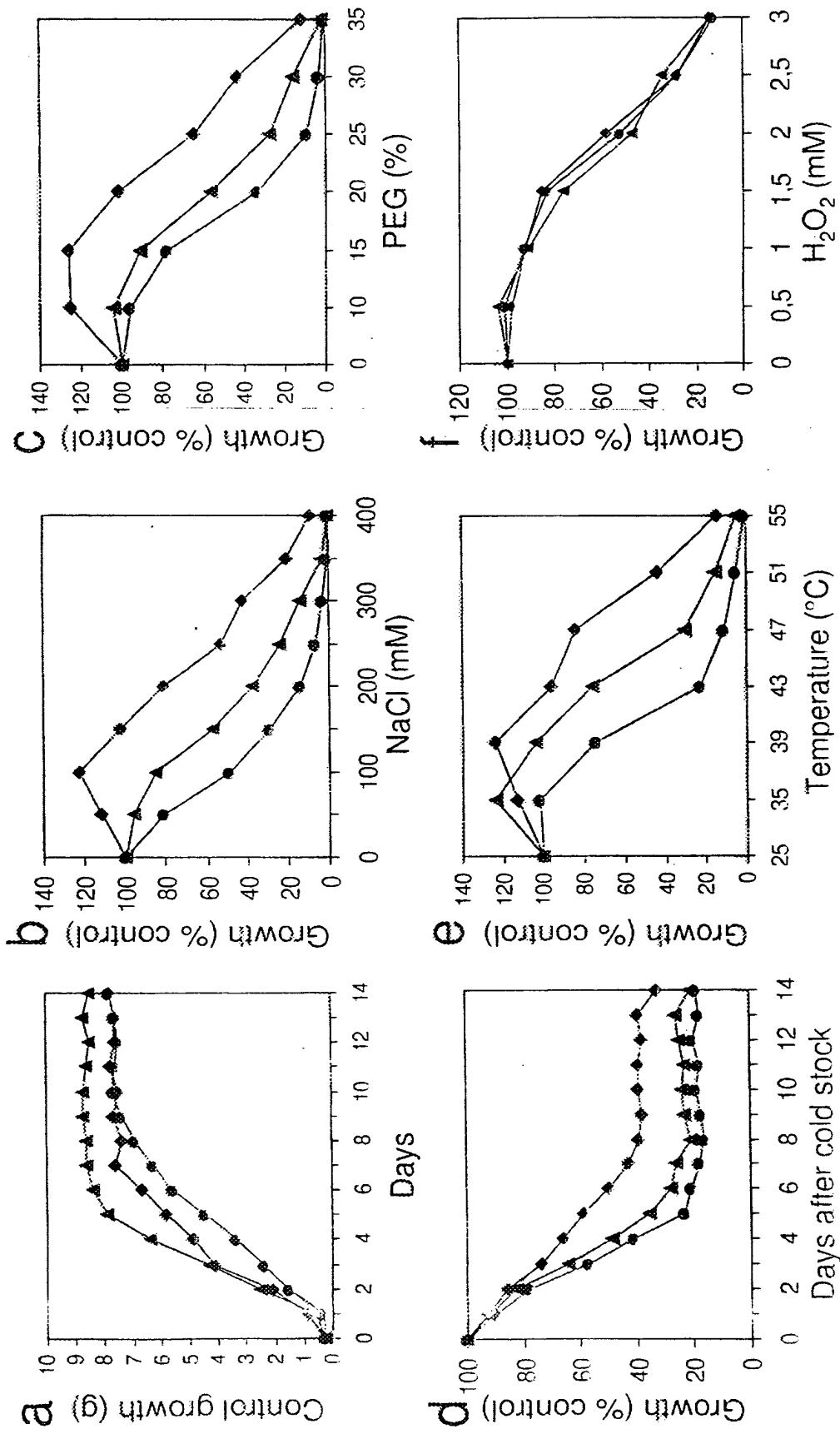


FIGURE 12B

14/15



FIGURE 13

15/15



FIGURE 14

SEQUENCE LISTING

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<120> Genes involved in tolerance to environmental stress

<130> VIB-14-NV/OSMO

<140>

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<150> 98202634.6

<151> 1998-08-04

<160> 126

<170> PatentIn Ver. 2.1

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<222> (40)..(1626)

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				1				5	

tcg	tgt	tta	agc	acg	gac	gga	cac	ggg	acc	cct	ggc	ggt	tca	ggg	cat	102
Ser	Cys	Leu	Ser	Thr	Asp	Gly	His	Gly	Thr	Pro	Gly	Gly	Ser	Gly	His	
				10			15						20			

tcc	ccc	aat	cag	aac	cta	acg	aaa	aga	aga	acg	cgt	cca	gct	ggg	atc	150
Phe	Pro	Asn	Gln	Asn	Leu	Thr	Lys	Arg	Arg	Thr	Arg	Pro	Ala	Gly	Ile	
				25			30						35			

aac	gac	tcg	cct	tcg	ccg	gtg	aaa	tgc	ttt	ttt	ttc	ccc	tat	gaa	gac	198
Asn	Asp	Ser	Pro	Ser	Pro	Val	Lys	Cys	Phe	Phe	Phe	Pro	Tyr	Glu	Asp	
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Thr	Ser	Asn	Thr	Ser	Leu	Lys	Glu	Val	Ser	Gln	Pro	Thr	Lys	Tyr	Ser	
				55			60						65			

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Ser	Asn	Ser	Pro	Pro	Val	Ser	Pro	Ala	Ile	Phe	Tyr	Glu	Arg	Ala	Thr	
				70			75						85			

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Ser	Trp	Cys	Thr	Gln	Arg	Val	Val	Ser	Gly	Arg	Ala	Met	Tyr	Phe	Leu	
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Glu	Tyr	Tyr	Cys	Asp	Met	Phe	Asp	Tyr	Val	Ile	Ser	Arg	Arg	Gln	Arg		
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Thr	Lys	Gln	Val	Leu	Glu	Tyr	Leu	Gln	Gln	Ser	Gln	Leu	Pro	Asn			
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Ser	Asp	Gln	Ile	Lys	Leu	Asn	Glu	Glu	Trp	Ser	Ser	Tyr	Leu	Gln	Arg		
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gag	cat	cag	gtt	ttg	tcg	aaa	aga	agg	ttg	aag	cca	aaa	aac	aga	gac		534
Glu	His	Gln	Val	Leu	Ser	Lys	Arg	Arg	Leu	Lys	Pro	Lys	Asn	Arg	Asp		
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Phe	Glu	Met	Ile	Thr	Gln	Val	Gly	Gln	Gly	Gly	Tyr	Gly	His	Val	Tyr		
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tta	gcc	aga	aag	aaa	gac	aca	aaa	gag	gtg	tgc	gcc	tta	aaa	att	ttg		630
Leu	Ala	Arg	Lys	Lys	Asp	Thr	Lys	Glu	Val	Cys	Ala	Leu	Lys	Ile	Leu		
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aat	aag	aag	cta	ggt	ttc	aaa	ctt	aat	ggt	aca	tgc	cat	gtt	ttg	acc		678
Asn	Lys	Lys	Leu	Gly	Phe	Lys	Leu	Asn	Gly	Thr	Cys	His	Val	Leu	Thr		
					200			205			210						
gag	agg	cag	agt	ctg	act	aca	acg	aga	tcc	gag	acg	atg	gtg	aag	ctc		726
Glu	Arg	Gln	Ser	Leu	Thr	Thr	Arg	Ser	Glu	Thr	Met	Val	Lys	Leu			
					215			220			225						
cta	agt	ggg	acg	acc	ccc	gta	ggc	agt	agg	ggg	atg	gcg	ata	gaa	agt		774
Leu	Ser	Gly	Thr	Thr	Pro	Val	Gly	Ser	Arg	Gly	Met	Ala	Ile	Glu	Ser		
					230		235			240		245					
gag	cta	ggc	ggt	gac	tcc	cgt	aca	gaa	agt	ata	gga	cgt	aga	tgc	ttg		822
Glu	Leu	Gly	Gly	Asp	Phe	Arg	Thr	Glu	Ser	Ile	Gly	Arg	Arg	Cys	Leu		
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aaa	agt	ggc	cat	gcf	aga	ttc	tat	att	agc	gaa	atg	tcc	tgt	gcc	gtc		870
Lys	Ser	Gly	His	Ala	Arg	Phe	Tyr	Ile	Ser	Glu	Met	Phe	Cys	Ala	Val		
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aac	gag	aaa	cat	ctt	tta	agt	aaa	acg	gac	agc	aca	atc	tcc	aac	gaa		918
Asn	Glu	Lys	His	Leu	Leu	Ser	Lys	Thr	Asp	Ser	Thr	Ile	Ser	Asn	Glu		
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tcg tcg acc aac gaa acg tat gcg atc agt cgt agc tgg aaa cag acg Ser Ser Thr Asn Glu Thr Tyr Ala Ile Ser Arg Ser Trp Lys Gln Thr 375	380	385	1206
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acg tgg gac ttg att acc aga cac agg gcc gac cta agc acg cgg acg Thr Trp Asp Leu Ile Thr Arg His Arg Ala Asp Leu Ser Thr Arg Thr 410	415	420	1302
aga tcc ttt gag cac gag gta aag atg agc tac ttc gcg gac atc ttg Arg Ser Phe Glu His Glu Val Lys Met Ser Tyr Phe Ala Asp Ile Leu 425	430	435	1350
ttt aag gcc tta aga tcg ata att cca cct ttc aca ccc caa cta gac Phe Lys Ala Leu Arg Ser Ile Ile Pro Pro Phe Thr Pro Gln Leu Asp 440	445	450	1398
agc gag acc gat gcc ggt tat ttc gat gac ttt tgg aat gag gct gac Ser Glu Thr Asp Ala Gly Tyr Phe Asp Asp Phe Trp Asn Glu Ala Asp 455	460	465	1446
ata gcc aaa tac gct gac gtc ttt aat agt cag tgc tgc cgt acg gct Ile Ala Lys Tyr Ala Asp Val Phe Asn Ser Gln Cys Cys Arg Thr Ala 470	475	480	1494
tta gtc gac gat tct gct gtt tct tct aaa ctt gtt ggg ttc acc ttc Leu Val Asp Asp Ser Ala Val Ser Ser Lys Leu Val Gly Phe Thr Phe 490	495	500	1542
cga cac aga aat ggt aaa cag ggt tcc agt ggt atg tta ttc aac ggg Arg His Arg Asn Gly Lys Gln Gly Ser Ser Gly Met Leu Phe Asn Gly 505	510	515	1590
cta gaa cac tca gac ccc ttc tca acc ttt tac tag taatcgccag Leu Glu His Ser Asp Pro Phe Ser Thr Phe Tyr 520	525		1636
cctgcaggcct gcccagctgc cagcctgccc tcgcctgacg cctgccccag gatgcctctc cttggataa catgcctgc tccccatgc cttgtgcct cgcaagcctga acgcctgcca gagctcgcca gcctgcccag ctttcgccc cagcctgcca gcctttttt aaacgctgaa aaacgcctaa aaaaatcgaa ctttaaacgc ttttaaaacg gctgcccata aaaaaaaaaagg			1696 1756 1816 1876

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1909

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35 40 45
Phe Pro Tyr Glu Asp Thr Ser Asn Thr Ser Leu Lys Glu Val Ser Gln
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Pro Thr Lys Tyr Ser Ser Asn Ser Pro Pro Val Ser Pro Ala Ile Phe
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Tyr Glu Arg Ala Thr Ser Trp Cys Thr Gln Arg Val Val Ser Gly Arg
85 90 95
Ala Met Tyr Phe Leu Glu Tyr Tyr Cys Asp Met Phe Asp Tyr Val Ile
100 105 110
Ser Arg Arg Gln Arg Thr Lys Gln Val Leu Glu Tyr Leu Gln Gln Gln
115 120 125
Ser Gln Leu Pro Asn Ser Asp Gln Ile Lys Leu Asn Glu Glu Trp Ser
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Ser Tyr Leu Gln Arg Glu His Gln Val Leu Ser Lys Arg Arg Leu Lys
145 150 155 160
Pro Lys Asn Arg Asp Phe Glu Met Ile Thr Gln Val Gly Gln Gly Gly
165 170 175
Tyr Gly His Val Tyr Leu Ala Arg Lys Lys Asp Thr Lys Glu Val Cys
180 185 190
Ala Leu Lys Ile Leu Asn Lys Lys Leu Gly Phe Lys Leu Asn Gly Thr
195 200 205
Cys His Val Leu Thr Glu Arg Gln Ser Leu Thr Thr Thr Arg Ser Glu
210 215 220
Thr Met Val Lys Leu Leu Ser Gly Thr Thr Pro Val Gly Ser Arg Gly
225 230 235 240
Met Ala Ile Glu Ser Glu Leu Gly Gly Asp Phe Arg Thr Glu Ser Ile
245 250 255

Gly Arg Arg Cys Leu Lys Ser Gly His Ala Arg Phe Tyr Ile Ser Glu
 260 265 270
 Met Phe Cys Ala Val Asn Glu Lys His Leu Leu Ser Lys Thr Asp Ser
 275 280 285
 Thr Ile Ser Asn Glu Glu Asp Ser Ser Ile Asn Ile Arg Leu Glu Lys
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 Phe Lys Asp Leu Gly Tyr Pro Ala Leu Ser Glu Lys Ser Ile Glu Asp
 305 310 315 320
 Arg Arg Lys Leu Tyr Thr Cys Pro Asn Ser Met Val Gly Ser Pro Asp
 325 330 335
 Tyr Ile Ala Leu Glu Val Leu Arg Gly Lys Arg Tyr Glu Tyr Thr Val
 340 345 350
 Asp Tyr Trp Ser Leu Gly Cys Met Leu Phe Glu Ser Leu Val Gly Tyr
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 Thr Pro Phe Ser Gly Ser Ser Thr Asn Glu Thr Tyr Ala Ile Ser Arg
 370 375 380
 Ser Trp Lys Gln Thr Leu Asn Arg Ala Arg His Glu Asp Gly Arg Ala
 385 390 395 400
 Ala Phe Tyr Asn Arg Thr Trp Asp Leu Ile Thr Arg His Arg Ala Asp
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 Leu Ser Thr Arg Thr Arg Ser Phe Glu His Glu Val Lys Met Ser Tyr
 420 425 430
 Phe Ala Asp Ile Leu Phe Lys Ala Leu Arg Ser Ile Ile Pro Pro Phe
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 Thr Pro Gln Leu Asp Ser Glu Thr Asp Ala Gly Tyr Phe Asp Asp Phe
 450 455 460
 Trp Asn Glu Ala Asp Ile Ala Lys Tyr Ala Asp Val Phe Asn Ser Gln
 465 470 475 480
 Cys Cys Arg Thr Ala Leu Val Asp Asp Ser Ala Val Ser Ser Lys Leu
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Met Asp Leu Glu Phe Gly Arg
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Phe Pro Ile Phe Ser Ile Leu Glu Asp Met Leu Glu Ala Pro Glu Glu
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caa acc gag aag act cgt aac aac cct tca aga gct tac atg cga gac 210
Gln Thr Glu Lys Thr Arg Asn Asn Pro Ser Arg Ala Tyr Met Arg Asp
25 30 35

gca aag gca atg gct gct aca cca gct gac gtt atc gag cac ccg gat 258
Ala Lys Ala Met Ala Ala Thr Pro Ala Asp Val Ile Glu His Pro Asp
40 45 50 55

gcg tac gtt ttc gcc gtg gac atg cct gga atc aaa gga gat gag att 306
Ala Tyr Val Phe Ala Val Asp Met Pro Gly Ile Lys Gly Asp Glu Ile
60 65 70

cag gtc cag ata gag aac gag aac gtg ctt gtg gtg agt ggc aaa aga 354
Gln Val Gln Ile Glu Asn Glu Asn Val Leu Val Val Ser Gly Lys Arg
75 80 85

cag agg gac aac aag gag aat gaa ggt gtg aag ttt gtg agg atg gag 402
Gln Arg Asp Asn Lys Glu Asn Glu Gly Val Lys Phe Val Arg Met Glu
90 95 100

agg agg atg ggg aag ttt atg agg aag ttt cag tta cct gat aat gca 450
Arg Arg Met Gly Lys Phe Met Arg Lys Phe Gln Leu Pro Asp Asn Ala
105 110 115

gat ttg gag aag atc tct gcg gct tgt aat gac ggt gtg ttg aaa gtg 498
Asp Leu Glu Lys Ile Ser Ala Ala Cys Asn Asp Gly Val Leu Lys Val
120 125 130 135

act att ccg aaa ctt cct cct gag cca aag aaa cca aag act ata 546
Thr Ile Pro Lys Leu Pro Pro Glu Pro Lys Lys Pro Lys Thr Ile
140 145 150

caa gtt caa gtc gct tga gtttgttgt gatccgtgtt tttgtgtttt 594
Gln Val Gln Val Ala
155

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Asp Val Ile Glu His Pro Asp Ala Tyr Val Phe Ala Val Asp Met Pro
 50 55 60

Gly Ile Lys Gly Asp Glu Ile Gln Val Gln Ile Glu Asn Glu Asn Val
 65 70 75 80

Leu Val Val Ser Gly Lys Arg Gln Arg Asp Asn Lys Glu Asn Glu Gly
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Val Lys Phe Val Arg Met Glu Arg Arg Met Gly Lys Phe Met Arg Lys
 100 105 110

Phe Gln Leu Pro Asp Asn Ala Asp Leu Glu Lys Ile Ser Ala Ala Cys
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 ttccaatcat cc atg agt ccg gac aat aaa ctg ctt ccg aag ccg atc atc 171
 Met Ser Pro Asp Asn Lys Leu Leu Pro Lys Arg Ile Ile
 1 5 10

ctt gta cgg cac ggt gaa tcg gaa ggg aat ctc gac acg gcg gcg tat	219
Leu Val Arg His Gly Glu Ser Glu Gly Asn Leu Asp Thr Ala Ala Tyr	
15 20 25	
aca acg acg ccg gat cat aag atc cag tta acg gat tcc ggt ttg ctt	267
Thr Thr Thr Pro Asp His Lys Ile Gln Leu Thr Asp Ser Gly Leu Leu	
30 35 40 45	
cag gcg cag gaa gcc gga gct cgt ctc cac gct ttg atc tct tct aat	315
Gln Ala Gln Glu Ala Gly Ala Arg Leu His Ala Leu Ile Ser Ser Asn	
50 55 60	
cct tct tca ccg gag tgg cgt gtg tac ttc tac gtt tcg ccg tac gat	363
Pro Ser Ser Pro Glu Trp Arg Val Tyr Phe Tyr Val Ser Pro Tyr Asp	
65 70 75	
cgg act cga tct acg ctc ccg gag atc gga cgg tcg ttc tcg cgt cgc	411
Arg Thr Arg Ser Thr Leu Arg Glu Ile Gly Arg Ser Phe Ser Arg Arg	
80 85 90	
cgt gtg att ggt gtt cgc gaa gaa tgt cgg att agg gaa cag gat ttt	459
Arg Val Ile Gly Val Arg Glu Glu Cys Arg Ile Arg Glu Gln Asp Phe	
95 100 105	
ggg aat ttt cag gtt aaa gag cga atg aga gca acg aaa aag gtc aga	507
Gly Asn Phe Gln Val Lys Glu Arg Met Arg Ala Thr Lys Lys Val Arg	
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Glu Arg Phe Gly Arg Phe Phe Tyr Arg Phe Pro Glu Gly Glu Ser Ala	
130 135 140	
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Ala Asp Val Phe Asp Arg Val Ser Ser Phe Leu Glu Ser Leu Trp Arg	
145 150 155	
gac att gac atg aac aga ctg cac atc aac ccg tct cat gag cta aac	651
Asp Ile Asp Met Asn Arg Leu His Ile Asn Pro Ser His Glu Leu Asn	
160 165 170	
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Phe Val Ile Val Ser His Gly Leu Thr Ser Arg Val Phe Leu Met Lys	
175 180 185	
tgg ttt aag tgg tca gtg gaa cag ttc gag gga cta aac aat cca ggg	747
Trp Phe Lys Trp Ser Val Glu Gln Phe Glu Gly Leu Asn Asn Pro Gly	
190 195 200 205	
aac agt gag atc aga gtg atg gaa tta gga caa ggc ggt gat tac agc	795
Asn Ser Glu Ile Arg Val Met Glu Leu Gly Gln Gly Gly Asp Tyr Ser	
210 215 220	
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Leu Ala Ile His His Thr Glu Glu Glu Leu Ala Thr Trp Gly Leu Ser	
225 230 235	
cca gag atg att gca gat caa aag tgg cgg gct aac gcg cat aaa ggc	891

Pro Glu Met Ile Ala Asp Gln Lys Trp Arg Ala Asn Ala His Lys Gly
 240 245 250
 gaa tgg aaa gaa gat tgt aag tgg tat ttt ggt gat ttc ttc gac cat 939
 Glu Trp Lys Glu Asp Cys Lys Trp Tyr Phe Gly Asp Phe Phe Asp His
 255 260 265
 atg gca gat tcc gat aaa gag tgc gag act gag gcc act gaa gat aga 987
 Met Ala Asp Ser Asp Lys Glu Cys Glu Thr Glu Ala Thr Glu Asp Arg
 270 275 280 285
 gaa gaa gaa gaa gaa gag ggg aaa agg gta aat ctg cta acg agt 1035
 Glu Glu Glu Glu Glu Gly Lys Arg Val Asn Leu Leu Thr Ser
 290 295 300
 tca gaa tat agc aat gag cca gag tta tac aat gga caa tgc tgc tga 1083
 Ser Glu Tyr Ser Asn Glu Pro Glu Leu Tyr Asn Gly Gln Cys Cys
 305 310 315
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 35 40 45
 Glu Ala Gly Ala Arg Leu His Ala Leu Ile Ser Ser Asn Pro Ser Ser
 50 55 60
 Pro Glu Trp Arg Val Tyr Phe Tyr Val Ser Pro Tyr Asp Arg Thr Arg
 65 70 75 80
 Ser Thr Leu Arg Glu Ile Gly Arg Ser Phe Ser Arg Arg Arg Val Ile
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 Gly Val Arg Glu Glu Cys Arg Ile Arg Glu Gln Asp Phe Gly Asn Phe
 100 105 110
 Gln Val Lys Glu Arg Met Arg Ala Thr Lys Lys Val Arg Glu Arg Phe
 115 120 125

Gly Arg Phe Phe Tyr Arg Phe Pro Glu Gly Glu Ser Ala Ala Asp Val
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 Phe Asp Arg Val Ser Ser Phe Leu Glu Ser Leu Trp Arg Asp Ile Asp
 145 150 155 160
 Met Asn Arg Leu His Ile Asn Pro Ser His Glu Leu Asn Phe Val Ile
 165 170 175
 Val Ser His Gly Leu Thr Ser Arg Val Phe Leu Met Lys Trp Phe Lys
 180 185 190
 Trp Ser Val Glu Gln Phe Glu Gly Leu Asn Asn Pro Gly Asn Ser Glu
 195 200 205
 Ile Arg Val Met Glu Leu Gly Gln Gly Asp Tyr Ser Leu Ala Ile
 210 215 220
 His His Thr Glu Glu Glu Leu Ala Thr Trp Gly Leu Ser Pro Glu Met
 225 230 235 240
 Ile Ala Asp Gln Lys Trp Arg Ala Asn Ala His Lys Gly Glu Trp Lys
 245 250 255
 Glu Asp Cys Lys Trp Tyr Phe Gly Asp Phe Phe Asp His Met Ala Asp
 260 265 270
 Ser Asp Lys Glu Cys Glu Thr Glu Ala Thr Glu Asp Arg Glu Glu Glu
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 15 20 25

aga ttg ttc aca gag aat ggc gcg tat gtg ata gtc gcg gat atc ctt	147
Arg Leu Phe Thr Glu Asn Gly Ala Tyr Val Ile Val Ala Asp Ile Leu	
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gat aat gaa ggc atc ctt gtg gcg gaa tcg atc ggt ggg tgt tac gtt	195
Asp Asn Glu Gly Ile Leu Val Ala Glu Ser Ile Gly Gly Cys Tyr Val	
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cat tgt gac gta tcg aag gag gct gat gtt gag gcg gca gtg gag cta	243
His Cys Asp Val Ser Lys Glu Ala Asp Val Glu Ala Ala Val Glu Leu	
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Ala Met Arg Arg Lys Gly Arg Leu Asp Val Met Phe Asn Asn Ala Gly	
80 85 90	
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Met Ser Leu Asn Glu Gly Ser Ile Met Gly Met Asp Val Asp Met Val	
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Asn Lys Leu Val Ser Val Asn Val Asn Gly Val Leu His Gly Ile Lys	
110 115 120	
cat gcc gct aag gcc atg atc aaa ggg gga cga gga ggc tcg ata ata	435
His Ala Ala Lys Ala Met Ile Lys Gly Gly Arg Gly Ser Ile Ile	
125 130 135	
tgc aca tcg agc tca tca ggg cta atg gga gga ctt gga gga cat gcg	483
Cys Thr Ser Ser Ser Gly Leu Met Gly Gly Leu Gly Gly His Ala	
140 145 150 155	
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Tyr Thr Leu Ser Lys Gly Gly Ile Asn Gly Val Val Arg Thr Thr Glu	
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Cys Glu Leu Gly Ser His Gly Ile Arg Val Asn Ser Ile Ser Pro His	
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Gly Val Pro Thr Asp Ile Leu Val Asn Ala Tyr Arg Lys Phe Leu Asn	
190 195 200	
aat gac aaa ctc aac gtc gct gag gtc acc gac att att gct gag aaa	675
Asn Asp Lys Leu Asn Val Ala Glu Val Thr Asp Ile Ile Ala Glu Lys	
205 210 215	
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Gly Ser Leu Leu Thr Gly Arg Ala Gly Thr Val Glu Asp Val Ala Gln	
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Gly Gly Ile Asn Gly Val Val Arg Thr Thr Glu Cys Glu Leu Gly Ser			
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Ile Leu Val Asn Ala Tyr Arg Lys Phe Leu Asn Asn Asp Lys Leu Asn			
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Val Ala Glu Val Thr Asp Ile Ile Ala Glu Lys Gly Ser Leu Leu Thr			
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225	230	235	240
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 ly Pro Val Leu
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 Phe Phe Glu Val Thr His Asp Ile Ser Asn Leu Thr Cys Ala Asp Phe
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 Val Val His Gly Arg Ala Ser Pro Glu Thr Met Arg Asp Ile Arg Gly
 110 115 120

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ttc atc cgt gat ggg att cag ttc ccg gat gtt gtc cac gcg ttg aaa Phe Ile Arg Asp Gly Ile Gln Phe Pro Asp Val Val His Ala Leu Lys 145 150 155	1664
cct aac cga aaa aca aac atc caa gag tac tgg agg att ctg gac tac Pro Asn Arg Lys Thr Asn Ile Gln Glu Tyr Trp Arg Ile Leu Asp Tyr 160 165 170 175	1712
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gat gtt ggt att cca caa gat tac agg cat atg gag ggt ttc ggt gtc Asp Val Gly Ile Pro Gln Asp Tyr Arg His Met Glu Gly Phe Gly Val 195 200 205	1808
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cac gat gcc att gca tct ggc aac tac ccc gag tgg aaa ctt ttc atc His Asp Ala Ile Ala Ser Gly Asn Tyr Pro Glu Trp Lys Leu Phe Ile 260 265 270	2000
cag acc atg gat cct gca gat gag gat aag ttt gac ttt gac cca ctt Gln Thr Met Asp Pro Ala Asp Glu Asp Lys Phe Asp Phe Asp Pro Leu 275 280 285	2048
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Gln Arg His Arg Leu Gly Pro Asn Tyr Leu Gln Leu Pro Val Asn Ala				
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ccc aaa tgt gct cac cac aac aat cac cat gaa ggt ttt atg aac ttc 2336				
Pro Lys Cys Ala His His Asn Asn His His Glu Gly Phe Met Asn Phe				
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atg cac aga gat gag gag gtacgtctta gtacaccact tgagctacca 2384				
Met His Arg Asp Glu Glu				
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			390	
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Thr His Glu Ile Arg Gly Ile Trp Thr Ser Tyr Trp Leu Lys				
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Lys Leu Ala Ser Arg Leu Asn Val Arg Pro Ser Ile				
485	490			

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Gln Thr Pro Val Ile Val Arg Phe Ser Thr Val Val His Gly Arg Ala
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Ser Pro Glu Thr Met Arg Asp Ile Arg Gly Phe Ala Val Lys Phe Tyr
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Thr Arg Glu Gly Asn Phe Asp Leu Val Gly Asn Asn Thr Pro Val Phe
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Pro Asn Arg Lys Thr Asn Ile Gln Glu Tyr Trp Arg Ile Leu Asp Tyr
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Met Ser His Leu Pro Glu Ser Leu Leu Thr Trp Cys Trp Met Phe Asp
 180 185 190

Asp Val Gly Ile Pro Gln Asp Tyr Arg His Met Glu Gly Phe Gly Val
 195 200 205

His Thr Tyr Thr Leu Ile Ala Lys Ser Gly Lys Val Leu Phe Val Lys
 210 215 220

Phe His Trp Lys Pro Thr Cys Gly Ile Lys Asn Leu Thr Asp Glu Glu

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Gln Thr Met Asp Pro Ala Asp Glu Asp Lys Phe Asp Phe Asp Pro Leu			
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Asp Val Thr Lys Ile Trp Pro Glu Asp Ile Leu Pro Leu Gln Pro Val			
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Glu Gln Leu Ala Phe Asn Pro Gly Leu Val Val Pro Gly Ile Tyr Tyr			
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Pro Lys Cys Ala His His Asn Asn His His Glu Gly Phe Met Asn Phe			
370	375	380	
Met His Arg Asp Glu Glu Ile Asn Tyr Tyr Pro Ser Lys Phe Asp Pro			
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Val Arg Cys Ala Glu Lys Val Pro Thr Pro Thr Asn Ser Tyr Thr Gly			
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Ile Arg Thr Lys Cys Val Ile Lys Lys Glu Asn Asn Phe Lys Gln Ala			
420	425	430	
Gly Asp Arg Tyr Arg Ser Trp Ala Pro Asp Arg Gln Asp Arg Phe Val			
435	440	445	
Lys Arg Trp Val Glu Ile Leu Ser Glu Pro Arg Leu Thr His Glu Ile			
450	455	460	
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      1           5           10

caa gct gag att aac cag ctt ctt agc ttg atc atc aac acg ttc tac      156
Gln Ala Glu Ile Asn Gln Leu Leu Ser Leu Ile Ile Asn Thr Phe Tyr
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agc aac aaa gaa atc ttc ctc cgt gag ctc atc agt aac tct tct gat      204
Ser Asn Lys Glu Ile Phe Leu Arg Glu Leu Ile Ser Asn Ser Ser Asp
      35          40          45

gtaagttcc cttcaaatact ctctctgact cggtgtgact cgtccgccttc ctatttctt 264
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aag agc aag ctc gat gga cag cct gaa ctc ttc att aga ttg gtt cct      604
Lys Ser Lys Leu Asp Gly Gln Pro Glu Leu Phe Ile Arg Leu Val Pro
      60           65           70

gac aag cct aat aag acg ctc tca att att gac agt ggt att ggc atg      652
Asp Lys Pro Asn Lys Thr Leu Ser Ile Ile Asp Ser Gly Ile Gly Met
      75           80           85           90

acc aaa gca ggtaacgaat caatgcctaa taatctctcg ttgggtgagat        701
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165 170 175	
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180 185	
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190 195 200	
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250 255 260 265	
ctc atc aac aag cag aaa ccg atc tgg ttg agg aag cca gaa gag atc Leu Ile Asn Lys Gln Lys Pro Ile Trp Leu Arg Lys Pro Glu Glu Ile	1395
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285 290 295	

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tcc aag gcc att ctc ttt gta cca aag aga gct ccg ttt gat ctc ttt	315	320	325	1539
Phe Lys Ala Ile Leu Phe Val Pro Lys Arg Ala Pro Phe Asp Leu Phe				
gac acg agg aag ttg aat aac atc aag ctt tat gtc agg agg gtg	330	335	340	1587
Asp Thr Arg Lys Lys Leu Asn Asn Ile Lys Leu Tyr Val Arg Arg Val				
ttc att atg gac aac tgt gaa gag cta atc cca gag tac ctc agc ttt	350	355	360	1635
Phe Ile Met Asp Asn Cys Glu Glu Leu Ile Pro Glu Tyr Leu Ser Phe				
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Val Lys Gly Val Val Asp Ser Asp Asp Leu Pro Leu Asn Ile Ser Arg				
gag acg ctt caa cag aac aag atc ctt aag gtg atc agg aag aat cta	380	385	390	1731
Glu Thr Leu Gln Gln Asn Lys Ile Leu Lys Val Ile Arg Lys Asn Leu				
gtg aag aag tgc att gag atg ttc aac gag att gct gag aac aaa gag	395	400	405	1779
Val Lys Lys Cys Ile Glu Met Phe Asn Glu Ile Ala Glu Asn Lys Glu				
gac tac acc aaa ttc tat gag gct ttc tcc aag aat ctc aaa ttg ggt	410	415	420	1827
Asp Tyr Thr Lys Phe Tyr Glu Ala Phe Ser Lys Asn Leu Lys Leu Gly				
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Ile His Glu Asp Ser Gln Asn Arg Gly Lys Ile Ala Asp Leu Leu Arg				
tac cac tcc aca aag agt ggt gat gaa atg acg acg ttc aaa gat tac	445	450	455	1923
Tyr His Ser Thr Lys Ser Gly Asp Glu Met Thr Ser Phe Lys Asp Tyr				
gtc aca agg atg aag gaa ggt caa aag gac att ttc tac atc act ggt	460	465	470	1971
Val Thr Arg Met Lys Glu Gly Gln Lys Asp Ile Phe Tyr Ile Thr Gly				
gaa agc aaa aag gcg gtg gag aat tcc ttc ttg gag agg ctg aag aag	475	480	485	2019
Glu Ser Lys Lys Ala Val Glu Asn Ser Phe Leu Glu Arg Leu Lys Lys				
aga ggc tac gag gta ctt tac atg gtg gat gcg att gac gaa tac gct	490	495	500	2067
Arg Gly Tyr Glu Val Leu Tyr Met Val Asp Ala Ile Asp Glu Tyr Ala				
gtt gga caa ttg aag gag tat gac ggt aag aaa ctt gtt tct gcg act	510	515	520	2115
Val Gly Gln Leu Lys Glu Tyr Asp Gly Lys Lys Leu Val Ser Ala Thr				
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Lys Glu Gly Leu Lys Leu Glu Asp Glu Thr Glu Glu Glu Lys Lys Lys			
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Arg Glu Glu Lys Lys Ser Phe Glu Asn Leu Cys Lys Thr Ile Lys			
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gaa att ctc ggg gac aag gtt gag aag gtt gtg gtc tca gac agg att		2259	
Glu Ile Leu Gly Asp Lys Val Glu Lys Val Val Val Ser Asp Arg Ile			
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Val Asp Ser Pro Cys Cys Leu Val Thr Gly Glu Tyr Gly Trp Thr Ala			
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Asn Met Glu Arg Ile Met Lys Ala Gln Ala Leu Arg Asp Ser Ser Met			
590	595	600	
agt ggt tac atg tcg agc aag aaa aca atg gag atc aac ccc gac aac		2403	
Ser Gly Tyr Met Ser Ser Lys Lys Thr Met Glu Ile Asn Pro Asp Asn			
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ggt ata atg gag gac ctc agg aag aga gct gaa gca gac aag aat gac		2451	
Gly Ile Met Glu Asp Leu Arg Lys Arg Ala Glu Ala Asp Lys Asn Asp			
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635	640	645	
acg tct gga ttt agt ctt gat gaa ccg aac act ttt gct gct agg att		2547	
Thr Ser Gly Phe Ser Leu Asp Glu Pro Asn Thr Phe Ala Ala Arg Ile			
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cac agg atg ttg aag ttg ggt ctg agt att gat gag gat gag aac gtt		2595	
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Gln Pro Glu Leu Phe Ile Arg Leu Val Pro Asp Lys Pro Asn Lys Thr
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Leu Ser Ile Ile Asp Ser Gly Ile Gly Met Thr Lys Ala Asp Leu Val
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Gly Phe Tyr Ser Ala Tyr Leu Val Ala Glu Lys Val Val Val Thr Thr
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His Phe Ser Val Glu Gly Gln Leu Glu Phe Lys Ala Ile Leu Phe Val
 305 310 315 320

Pro Lys Arg Ala Pro Phe Asp Leu Phe Asp Thr Arg Lys Lys Leu Asn
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 Arg Gly Lys Ile Ala Asp Leu Leu Arg Tyr His Ser Thr Lys Ser Gly
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Glu Pro Asn Thr Phe Ala Ala Arg Ile His Arg Met Leu Lys Leu Gly
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Leu Glu Glu Leu Gly Ser Val Leu Thr Ser Leu Asp Pro Gly Asp Ser	
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agg ata agg gac tgt ctt gct caa ctc tat gca aag gac att act cct Arg Ile Arg Asp Cys Leu Ala Gln Leu Tyr Ala Lys Asp Ile Thr Pro 190	195	200	626
gat gac aag cag gag cta gat gag tct ctg caa aga gag att caa gct Asp Asp Lys Gln Glu Leu Asp Glu Ser Leu Gln Arg Glu Ile Gln Ala 205	210	215	674
gca ttc cga aca gat gag att aga aga aca cct cca acc cca caa gat Ala Phe Arg Thr Asp Glu Ile Arg Arg Thr Pro Pro Thr Pro Gln Asp 220	225	230	722
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tgg atg ggc ggt gat cgt gat ggt aat ccg agg gtc aca cct gag gtc Trp Met Gly Gly Asp Arg Asp Gly Asn Pro Arg Val Thr Pro Glu Val 285	290	295	914
act aga gat gtg tgc ttg ttg gct aga atg atg gct gcc aat ctc tac Thr Arg Asp Val Cys Leu Leu Ala Arg Met Met Ala Ala Asn Leu Tyr 300	305	310	962
tat aac caa atc gag aat ctg atg ttt gag tta tct atg tgg cgt tgc Tyr Asn Gln Ile Glu Asn Leu Met Phe Glu Leu Ser Met Trp Arg Cys 320	325	330	1010
act gat gaa ttc cgt gtg cgg gcg gat gaa ctg cac agg aac tca agg Thr Asp Glu Phe Arg Val Arg Ala Asp Glu Leu His Arg Asn Ser Arg 335	340	345	1058

aaa gat gct gca aaa cat tac ata gaa ttc tgg aag aca att cct cca		1106
Lys Asp Ala Ala Lys His Tyr Ile Glu Phe Trp Lys Thr Ile Pro Pro		
350	355	360
act gag cca tac cgt gtg att ctt ggt gat gtg agg gat aag ctg tat		1154
Thr Glu Pro Tyr Arg Val Ile Leu Gly Asp Val Arg Asp Lys Leu Tyr		
365	370	375
cac aca cgt gag cgt tcc cgc caa ttg ctg agt aat gga atc tcg gat		1202
His Thr Arg Glu Arg Ser Arg Gln Leu Leu Ser Asn Gly Ile Ser Asp		
380	385	390
395		
att cct gaa gaa gct acc ttc act aat gtg gaa cag ttc ttg gag cct		1250
Ile Pro Glu Glu Ala Thr Phe Thr Asn Val Glu Gln Phe Leu Glu Pro		
400	405	410
ctt gag ctc tgt tac cga tca cta tgt tca tgt ggt gac agc ccg ata		1298
Leu Glu Leu Cys Tyr Arg Ser Leu Cys Ser Cys Gly Asp Ser Pro Ile		
415	420	425
430	435	440
gct gat gga agc ctt ctt gat ttc ttg agg caa gtc tct acc ttt gga		1346
Ala Asp Gly Ser Leu Leu Asp Phe Leu Arg Gln Val Ser Thr Phe Gly		
445	450	455
460	465	470
475		
ctc tcc ctt gtg aga ctt gac atc agg caa gag tct gaa cgc cac aca		1394
Leu Ser Leu Val Arg Leu Asp Ile Arg Gln Glu Ser Glu Arg His Thr		
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500	505	
510	515	520
525	530	535
540	545	550
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gat gca ggg cgt ctc tca gct tgg gag cta tac aaa gct caa gaa Asp Ala Gly Arg Leu Ser Ala Ala Trp Glu Leu Tyr Lys Ala Gln Glu 605 610 615	1874
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cat ggc cgt ggt ggc aca gtc gga aga gga ggt ggt cct act cat ctt His Gly Arg Gly Thr Val Gly Arg Gly Gly Pro Thr His Leu 640 645 650	1970
gct ata ttg tct cag cca cca gat aca gtt aat ggc tct ctt cga gtc Ala Ile Leu Ser Gln Pro Pro Asp Thr Val Asn Gly Ser Leu Arg Val 655 660 665	2018
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atg aac cct ccg att tca cca aaa ccc gag tgg cgt gct ttg ctt gat Met Asn Pro Pro Ile Ser Pro Lys Pro Glu Trp Arg Ala Leu Leu Asp 700 705 710 715	2162
gaa atg gcg gtt gtt gca act gag gaa tac cga tct gtc gtt ttc caa Glu Met Ala Val Val Ala Thr Glu Glu Tyr Arg Ser Val Val Phe Gln 720 725 730	2210
gaa cct cga ttc gtc gag tat ttc cgc ctc gct act ccg gag ctg gag Glu Pro Arg Phe Val Glu Tyr Phe Arg Leu Ala Thr Pro Glu Leu Glu 735 740 745	2258
tat gga cgt atg aat att gga agt aga cct tca aag cga aaa cca agc Tyr Gly Arg Met Asn Ile Gly Ser Arg Pro Ser Lys Arg Lys Pro Ser 750 755 760	2306
ggg ggg atc gaa tct ctc cgt gca atc cca tgg atc ttt gct tgg acg Gly Gly Ile Glu Ser Leu Arg Ala Ile Pro Trp Ile Phe Ala Trp Thr 765 770 775	2354
caa aca aga ttc cat ctt cct gta tgg tta ggt ttc gga gca gca ttt Gln Thr Arg Phe His Leu Pro Val Trp Leu Gly Phe Gly Ala Ala Phe 780 785 790 795	2402
agg tat gcg atc aag aag gat gtg aga aac ctt cac atg ctg caa gat	2450

Arg Tyr Ala Ile Lys Lys Asp Val Arg Asn Leu His Met Leu Gln Asp			
800	805	810	
atg tat aaa caa tgg ccc ttt ttc cga gtc acc atc gat cta att gaa	2498		
Met Tyr Lys Gln Trp Pro Phe Phe Arg Val Thr Ile Asp Leu Ile Glu			
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Met Val Phe Ala Lys Gly Asp Pro Gly Ile Ala Ala Leu Tyr Asp Lys			
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ctt ctt gtc tca gaa gat tta tgg gct ttt gga gag aaa ctc aga gcc	2594		
Leu Leu Val Ser Glu Asp Leu Trp Ala Phe Gly Glu Lys Leu Arg Ala			
845	850	855	
aac ttt gat gaa acc aag aac ctc gtc ctc cag act gct gga cat aaa	2642		
Asn Phe Asp Glu Thr Lys Asn Leu Val Leu Gln Thr Ala Gly His Lys			
860	865	870	875
gac ctt ctt gaa gga gat cct tac ttg aaa cag aga cta agg cta cgt	2690		
Asp Leu Leu Glu Gly Asp Pro Tyr Leu Lys Gln Arg Leu Arg Leu Arg			
880	885	890	
gac tct tac att acg acc ctc aac gtt tgc caa gcc tac aca ttg aag	2738		
Asp Ser Tyr Ile Thr Thr Leu Asn Val Cys Gln Ala Tyr Thr Leu Lys			
895	900	905	
agg atc cgt gat gca aac tac aat gtg act ctg cga cca cac att tct	2786		
Arg Ile Arg Asp Ala Asn Tyr Asn Val Thr Leu Arg Pro His Ile Ser			
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aaa gag atc atgcaa tca agc aaa tca gca caa gag ctc gtc aag ctt	2834		
Lys Glu Ile Met Gln Ser Ser Lys Ser Ala Gln Glu Leu Val Lys Leu			
925	930	935	
aac ccc acg agt gaa tac gcg cct gga ctt gag gac aca ctt atc tta	2882		
Asn Pro Thr Ser Glu Tyr Ala Pro Gly Leu Glu Asp Thr Leu Ile Leu			
940	945	950	955
acc atg aag ggt att gct gca gga ttg caa aac acc ggt taa gtgagtca	2932		
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Ala Glu Tyr Glu Gly Lys Arg Glu Pro Ser Lys Leu Glu Glu Leu Gly			
65	70	75	80
Ser Val Leu Thr Ser Leu Asp Pro Gly Asp Ser Ile Val Ile Ser Lys			
85	90	95	
Ala Phe Ser His Met Leu Asn Leu Ala Asn Leu Ala Glu Glu Val Gln			
100	105	110	
Ile Ala His Arg Arg Arg Ile Lys Lys Leu Lys Lys Gly Asp Phe Val			
115	120	125	
Asp Glu Ser Ser Ala Thr Thr Glu Ser Asp Ile Glu Glu Thr Phe Lys			
130	135	140	
Arg Leu Val Ser Asp Leu Gly Lys Ser Pro Glu Glu Ile Phe Asp Ala			
145	150	155	160
Leu Lys Asn Gln Thr Val Asp Leu Val Leu Thr Ala His Pro Thr Gln			
165	170	175	
Ser Val Arg Arg Ser Leu Leu Gln Lys His Gly Arg Ile Arg Asp Cys			
180	185	190	
Leu Ala Gln Leu Tyr Ala Lys Asp Ile Thr Pro Asp Asp Lys Gln Glu			
195	200	205	
Leu Asp Glu Ser Leu Gln Arg Glu Ile Gln Ala Ala Phe Arg Thr Asp			
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Glu Ile Arg Arg Thr Pro Pro Thr Pro Gln Asp Glu Met Arg Ala Gly			
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Met Ser Tyr Phe His Glu Thr Ile Trp Lys Gly Val Pro Lys Phe Leu			
245	250	255	
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Pro Tyr Asn Ala Pro Leu Ile Gln Phe Ser Ser Trp Met Gly Gly Asp			
275	280	285	
Arg Asp Gly Asn Pro Arg Val Thr Pro Glu Val Thr Arg Asp Val Cys			
290	295	300	
Leu Leu Ala Arg Met Met Ala Ala Asn Leu Tyr Tyr Asn Gln Ile Glu			
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Asn Leu Met Phe Glu Leu Ser Met Trp Arg Cys Thr Asp Glu Phe Arg			
325	330	335	
Val Arg Ala Asp Glu Leu His Arg Asn Ser Arg Lys Asp Ala Ala Lys			

340	345	350
His Tyr Ile Glu Phe Trp Lys Thr Ile Pro Pro Thr Glu Pro Tyr Arg		
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Val Ile Leu Gly Asp Val Arg Asp Lys Leu Tyr His Thr Arg Glu Arg		
370	375	380
Ser Arg Gln Leu Leu Ser Asn Gly Ile Ser Asp Ile Pro Glu Glu Ala		
385	390	395 400
Thr Phe Thr Asn Val Glu Gln Phe Leu Glu Pro Leu Glu Leu Cys Tyr		
405	410	415
Arg Ser Leu Cys Ser Cys Gly Asp Ser Pro Ile Ala Asp Gly Ser Leu		
420	425	430
Leu Asp Phe Leu Arg Gln Val Ser Thr Phe Gly Leu Ser Leu Val Arg		
435	440	445
Leu Asp Ile Arg Gln Glu Ser Glu Arg His Thr Asp Val Leu Asp Ala		
450	455	460
Ile Thr Lys His Leu Asp Ile Gly Ser Ser Tyr Arg Asp Trp Ser Glu		
465	470	475 480
Glu Gly Arg Gln Glu Trp Leu Leu Ala Glu Leu Ser Gly Lys Arg Pro		
485	490	495
Leu Phe Gly Pro Asp Leu Pro Lys Thr Glu Glu Ile Ser Asp Val Leu		
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Asp Thr Phe Lys Val Ile Ser Glu Leu Pro Ser Asp Cys Phe Gly Ala		
515	520	525
Tyr Ile Ile Ser Met Ala Thr Ser Pro Ser Asp Val Leu Ala Val Glu		
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Leu Phe Glu Lys Leu Ala Asp Leu Glu Ala Ala Pro Ala Ala Val Ala		
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Glu Val Met Ile Gly Tyr Ser Asp Ser Gly Lys Asp Ala Gly Arg Leu		
595	600	605
Ser Ala Ala Trp Glu Leu Tyr Lys Ala Gln Glu Glu Leu Val Lys Val		
610	615	620
Ala Lys Lys Tyr Gly Val Lys Leu Thr Met Phe His Gly Arg Gly Gly		
625	630	635 640
Thr Val Gly Arg Gly Gly Pro Thr His Leu Ala Ile Leu Ser Gln		

645	650	655
Pro Pro Asp Thr Val Asn Gly Ser Leu Arg Val Thr Val Gln Gly Glu		
660	665	670
Val Ile Glu Gln Ser Phe Gly Glu Ala His Leu Cys Phe Arg Thr Leu		
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Gln Arg Phe Thr Ala Ala Thr Leu Glu His Gly Met Asn Pro Pro Ile		
690	695	700
Ser Pro Lys Pro Glu Trp Arg Ala Leu Leu Asp Glu Met Ala Val Val		
705	710	715
Ala Thr Glu Glu Tyr Arg Ser Val Val Phe Gln Glu Pro Arg Phe Val		
725	730	735
Glu Tyr Phe Arg Leu Ala Thr Pro Glu Leu Glu Tyr Gly Arg Met Asn		
740	745	750
Ile Gly Ser Arg Pro Ser Lys Arg Lys Pro Ser Gly Gly Ile Glu Ser		
755	760	765
Leu Arg Ala Ile Pro Trp Ile Phe Ala Trp Thr Gln Thr Arg Phe His		
770	775	780
Leu Pro Val Trp Leu Gly Phe Gly Ala Ala Phe Arg Tyr Ala Ile Lys		
785	790	795
Lys Asp Val Arg Asn Leu His Met Leu Gln Asp Met Tyr Lys Gln Trp		
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Pro Phe Phe Arg Val Thr Ile Asp Leu Ile Glu Met Val Phe Ala Lys		
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Gly Asp Pro Gly Ile Ala Ala Leu Tyr Asp Lys Leu Leu Val Ser Glu		
835	840	845
Asp Leu Trp Ala Phe Gly Glu Lys Leu Arg Ala Asn Phe Asp Glu Thr		
850	855	860
Lys Asn Leu Val Leu Gln Thr Ala Gly His Lys Asp Leu Leu Glu Gly		
865	870	875
Asp Pro Tyr Leu Lys Gln Arg Leu Arg Leu Arg Asp Ser Tyr Ile Thr		
885	890	895
Thr Leu Asn Val Cys Gln Ala Tyr Thr Leu Lys Arg Ile Arg Asp Ala		
900	905	910
Asn Tyr Asn Val Thr Leu Arg Pro His Ile Ser Lys Glu Ile Met Gln		
915	920	925
Ser Ser Lys Ser Ala Gln Glu Leu Val Lys Leu Asn Pro Thr Ser Glu		
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gga tct gct gta gta gct tac gtg tgt gac aaa gtt att tct gat gat 100			
Gly Ser Ala Val Val Ala Tyr Val Cys Asp Lys Val Ile Ser Asp Asp			
15	20	25	
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Lys Leu Phe Gly Gly Thr Thr Pro Gly Thr Ile Asn Lys Glu Trp			
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ggc gct gct act gaa gag aga tta caa gca tgg cca aga gtt gct ggt 196			
Gly Ala Ala Thr Glu Glu Arg Leu Gln Ala Trp Pro Arg Val Ala Gly			
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cct ccc gtc gtc atg aac cct atc agt cgc cag aat ttc atc gtc aag 244			
Pro Pro Val Val Met Asn Pro Ile Ser Arg Gln Asn Phe Ile Val Lys			
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Gly Thr Thr Pro Gly Thr Ile Thr Asn Lys Glu Trp Gly Ala Ala Thr			
35	40	45	

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Glu Tyr Leu Lys Glu Ile Thr Lys Ala Arg Arg Glu Leu Arg Ser Leu
10 15 20

atc gcg aac aag aac tgt gct cct atc atg ctc cga ttg gcg 143
 Ile Ala Asn Lys Asn Cys Ala Pro Ile Met Leu Arg Leu Ala
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taagtttgcg atttccttgg ttttcgtcg agttgactgt tacagatttc gtttattcat 203
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 Trp His Asp Ala Gly Thr Tyr
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 Asp Ala Gln Ser Lys Thr Gly Gly Pro Asn Gly Ser Ile Arg Asn Glu
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 Glu Glu His Thr His Gly Ala Asn Ser Gly Leu Lys Ile Ala Leu Asp
 65 70 75

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 Glu
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 Gly Val Lys Ala Lys His Pro Lys Ile Thr Tyr Ala Asp Leu Tyr Gln
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Phe Gln His Leu Arg Asp Val Phe Tyr Arg Met Gly
140 145

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Leu Ser Asp Lys Asp Ile Val Ala Leu Ser Gly Gly His Thr Leu
150 155 160

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Gly Arg Ala His Pro Glu Arg Ser Gly Phe
165 170

gat gga cca tgg acc caa gag ccg ctg aat ttt gac aac tcc tac ttc 1738
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175 180 185

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200 205 210

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215 220

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 Asp Glu Asp Ala Phe Phe Arg Asp Tyr Ala Glu Ser His Lys Lys
 225 230 235
 ctc tct gag ctt ggt ttc aac cca aac tcc tca gca ggc aaa gca gtt 2462
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 35 40 45

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 50 55 60

 Thr His Gly Ala Asn Ser Gly Leu Lys Ile Ala Leu Asp Leu Cys Glu
 65 70 75 80

 Gly Val Lys Ala Lys His Pro Lys Ile Thr Tyr Ala Asp Leu Tyr Gln
 85 90 95

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 100 105 110

 Phe Val Pro Gly Arg Lys Asp Ser Asn Val Cys Pro Lys Glu Gly Arg
 115 120 125

 Leu Pro Asp Ala Lys Gln Gly Phe Gln His Leu Arg Asp Val Phe Tyr
 130 135 140

Arg Met Gly Leu Ser Asp Lys Asp Ile Val Ala Leu Ser Gly Gly His
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 Thr Leu Gly Arg Ala His Pro Glu Arg Ser Gly Phe Asp Gly Pro Trp
 165 170 175
 Thr Gln Glu Pro Leu Asn Phe Asp Asn Ser Tyr Phe Val Arg Glu Leu
 180 185 190
 Leu Lys Gly Glu Ser Glu Gly Leu Leu Lys Leu Pro Thr Asp Lys Thr
 195 200 205
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 210 215 220
 Glu Asp Ala Phe Phe Arg Asp Tyr Ala Glu Ser His Lys Lys Leu Ser
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 Glu Leu Gly Phe Asn Pro Asn Ser Ser Ala Gly Lys Ala Val Ala Asp
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Ser	Glu	Leu	Arg	Pro	His	Ala	Gly	Gly	Asp	Tyr	Ser	Ile	Ala	Val	Val		
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caa gcc aat tcc agg ctt gaa gat cag agt cag gtt ttc aca tct tct															196		
Gln	Ala	Asn	Ser	Arg	Leu	Glu	Asp	Gln	Ser	Gln	Val	Phe	Thr	Ser	Ser		
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tct gct act tac gtc ggt gta tac gat ggt cat ggt gga cct gaa gct															244		
Ser	Ala	Thr	Tyr	Val	Gly	Val	Tyr	Asp	Gly	His	Gly	Gly	Pro	Glu	Ala		
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tct aga ttc gtt aac aga cat ctc ttt cct tat atg cac a gtaagttata															294		
Ser	Arg	Phe	Val	Asn	Arg	His	Leu	Phe	Pro	Tyr	Met	His	L				
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Gly	Ala	Val	Ala	Glu	Arg	Leu	Ser	Thr	Asp	His	Asn	Val	Ala	Val	Glu		
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Val Ser Arg Ser Ile 215			
ggg gat gta tac ttg aaa aaa ccg gag tat tac agg gac ccg att ttc 1319			
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Gly Ile Ile Gln Val Ser Arg Ser Ile Gly Asp Val Tyr Leu Lys Lys	
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Lys	Gly	Ile	Arg	Arg	His	Phe	His	Asp	Asp	Ile	Ser	Val	Ile	Val	Val
						325			330			335			
Tyr	Leu	Asp	Gln	Asn	Lys	Thr	Ser	Ser	Ser	Asn	Ser	Lys	Leu	Val	Lys
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10 15 20
gat tgg tct tcc gct atg gat aag gaa gac gaa gtt ccc gag ctc gag 151
Asp Trp Ser Ser Ala Met Asp Lys Glu Asp Glu Val Pro Glu Leu Glu
25 30 35
att gtt aat acc acc aaa cct act cct ccg cca ccg cca acg ttt ttc 199
Ile Val Asn Thr Thr Lys Pro Thr Pro Pro Pro Pro Thr Phe Phe
40 45 50
tcc gac gat caa acc gat tct ccg aaa ctc cta acc gat cgt gac ctc 247
Ser Asp Asp Gln Thr Asp Ser Pro Lys Leu Leu Thr Asp Arg Asp Leu
55 60 65
gac gag cag cta gag cgt aaa aaa gcg atc ctg aca tta ggt ccg ggc 295
Asp Glu Gln Leu Glu Arg Lys Lys Ala Ile Leu Thr Leu Gly Pro Gly
70 75 80 85
tta ccc gac aag ggt gag aaa att cga ctc aaa atc gct gat ctc gaa 343
Leu Pro Asp Lys Gly Glu Lys Ile Arg Leu Lys Ile Ala Asp Leu Glu
90 95 100
gag gag aag cag c gtagagttt agaaggctcg aaaatggttc gcattctgat 396
Glu Glu Lys Gln A
105

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305 310 315

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Lys Thr Cys Ser Leu Gln Glu Asp Ile Cys Tyr Pro Thr ArSe
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Thr Leu Gly Pro Gly Leu Pro Asp Lys Gly Glu Lys Ile Arg Leu Lys			
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Gln Gln Ile Ser Sr Ser Asn Gln Ile Ser Ala Asp Cys His Phe Phe			
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Asn Asp Lys Ap Ala Phe Phe Val Arg Phe Arg Arg Trp Trp Lys Gly			
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Lys Ser Ile Val Glu Asn Val Lys Arg Phe Leu Lys Asp Glu Trp Asn			
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1		5	10
ggc act cgc ttg aga cca ttg act ctc agt ttc cca aag ccc ctt gtt 99			
Gly Thr Arg Leu Arg Pro Leu Thr Leu Ser Phe Pro Lys Pro Leu Val			
15		20	25
gat ttt gct aat aaa ccc atg atc ctt cat cag ata gag gct ctt aag 147			
Asp Phe Ala Asn Lys Pro Met Ile Leu His Gln Ile Glu Ala Leu Lys			
30		35	40
gca gtt gga gtt gat gaa gtg gtt ttg gcc atc aat tat cag cca gag 195			
Ala Val Gly Val Asp Glu Val Val Leu Ala Ile Asn Tyr Gln Pro Glu			
45		50	55
gtg atg ctg aac ttc ttg aag gac ttt gag acc aag ctg gaa atc aaa 243			
Val Met Leu Asn Phe Leu Lys Asp Phe Glu Thr Lys Leu Glu Ile Lys			
60		65	70
atc act tgc tca caa gag acc gag cca cta ggt acc gct ggt cct ctg 291			
Ile Thr Cys Ser Gln Glu Thr Glu Pro Leu Gly Thr Ala Gly Pro Leu			
75		80	85
gct cta gcg aga gac aaa ttg ctt gat gga tct gga gag ccc ttc ttt 339			
Ala Leu Ala Arg Asp Lys Leu Leu Asp Gly Ser Gly Glu Pro Phe Phe			

95	100	105	
gtt ctt aac agt gat gtg att agt gag tac cct ctt aaa gaa atg ctt Val Leu Asn Ser Asp Val Ile Ser Glu Tyr Pro Leu Lys Glu Met Leu 110	115	120	387
gag ttt cac aaa tct cac ggt ggg gaa gcc tcc ata atg gta aca aag Glu Phe His Lys Ser His Gly Gly Glu Ala Ser Ile Met Val Thr Lys 125	130	135	435
gtg gat gaa ccg tcg aaa tat gga gtg gtt atg gaa gaa agc act Val Asp Glu Pro Ser Lys Tyr Gly Val Val Val Met Glu Glu Ser Thr 140	145	150	483
gga aga gtg gag aag ttt gtg gaa aag cca aaa ctg tat gta ggt aac Gly Arg Val Glu Lys Phe Val Glu Lys Pro Lys Leu Tyr Val Gly Asn 155	160	165	531
aag atc aac gct ggg att tat ctt ctg aac cca tct gtt ctt gat aag Lys Ile Asn Ala Gly Ile Tyr Leu Leu Asn Pro Ser Val Leu Asp Lys 175	180	185	579
att gag cta aga ccg act tca atc gaa aaa gag act ttc cct aag att Ile Glu Leu Arg Pro Thr Ser Ile Glu Lys Glu Thr Phe Pro Lys Ile 190	195	200	627
gca gca gcg caa ggg ctc tat gct atg gtg cta cca ggg ttt tgg atg Ala Ala Ala Gln Gly Leu Tyr Ala Met Val Leu Pro Gly Phe Trp Met 205	210	215	675
gac att ggg caa ccc cgt gac tac ata acg ggt ttg aga ctc tac tta Asp Ile Gly Gln Pro Arg Asp Tyr Ile Thr Gly Leu Arg Leu Tyr Leu 220	225	230	723
gac tcc ctt agg aag aaa tct cct gcc aaa tta acc agt ggg cca cac Asp Ser Leu Arg Lys Lys Ser Pro Ala Lys Leu Thr Ser Gly Pro His 235	240	245	771
ata gtt ggg aat gtt ctt gtt gac gaa acc gct aca att ggg gaa gga Ile Val Gly Asn Val Leu Val Asp Glu Thr Ala Thr Ile Gly Glu Gly 255	260	265	819
tgt ttg att gga cca gac gtt gcc att ggt cca ggc tgc att gtt gag Cys Leu Ile Gly Pro Asp Val Ala Ile Gly Pro Gly Cys Ile Val Glu 270	275	280	867
tca gga gtc aga ctc tcc cga tgc acg gtc atg cgt gga gtc cgc atc Ser Gly Val Arg Leu Ser Arg Cys Thr Val Met Arg Gly Val Arg Ile 285	290	295	915
aag aag cat gcg tgt atc tcg agc agt atc atc ggg tgg cac tca acg Lys Lys His Ala Cys Ile Ser Ser Ile Ile Gly Trp His Ser Thr 300	305	310	963
gtt ggt caa tgg gcc agg atc gag aac atg acg atc ctc ggt gag gat Val Gly Gln Trp Ala Arg Ile Glu Asn Met Thr Ile Leu Gly Glu Asp 315	320	325	1011
			330

gtt cat gtg agc gat gag atc tat agc aat gga gga gtt gtt ttc cca	1059
Val His Val Ser Asp Glu Ile Tyr Ser Asn Gly Gly Val Val Leu Pro	
335 340 345	
cac aag gag atc aaa tca aac atc ttg aag cca gag ata gtg atg tga	1107
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Met Ile Leu His Gln Ile Glu Ala Leu Lys Ala Val Gly Val Asp Glu	
35 40 45	
Val Val Leu Ala Ile Asn Tyr Gln Pro Glu Val Met Leu Asn Phe Leu	
50 55 60	
Lys Asp Phe Glu Thr Lys Leu Glu Ile Lys Ile Thr Cys Ser Gln Glu	
65 70 75 80	
Thr Glu Pro Leu Gly Thr Ala Gly Pro Leu Ala Leu Ala Arg Asp Lys	
85 90 95	
Leu Leu Asp Gly Ser Gly Glu Pro Phe Phe Val Leu Asn Ser Asp Val	
100 105 110	
Ile Ser Glu Tyr Pro Leu Lys Glu Met Leu Glu Phe His Lys Ser His	
115 120 125	
Gly Gly Glu Ala Ser Ile Met Val Thr Lys Val Asp Glu Pro Ser Lys	
130 135 140	
Tyr Gly Val Val Val Met Glu Glu Ser Thr Gly Arg Val Glu Lys Phe	
145 150 155 160	
Val Glu Lys Pro Lys Leu Tyr Val Gly Asn Lys Ile Asn Ala Gly Ile	
165 170 175	
Tyr Leu Leu Asn Pro Ser Val Leu Asp Lys Ile Glu Leu Arg Pro Thr	
180 185 190	
Ser Ile Glu Lys Glu Thr Phe Pro Lys Ile Ala Ala Gln Gly Leu	
195 200 205	

Tyr Ala Met Val Leu Pro Gly Phe Trp Met Asp Ile Gly Gln Pro Arg
 210 215 220
 Asp Tyr Ile Thr Gly Leu Arg Leu Tyr Leu Asp Ser Leu Arg Lys Lys
 225 230 235 240
 Ser Pro Ala Lys Leu Thr Ser Gly Pro His Ile Val Gly Asn Val Leu
 245 250 255
 Val Asp Glu Thr Ala Thr Ile Gly Glu Gly Cys Leu Ile Gly Pro Asp
 260 265 270
 Val Ala Ile Gly Pro Gly Cys Ile Val Glu Ser Gly Val Arg Leu Ser
 275 280 285
 Arg Cys Thr Val Met Arg Gly Val Arg Ile Lys Lys His Ala Cys Ile
 290 295 300
 Ser Ser Ser Ile Ile Gly Trp His Ser Thr Val Gly Gln Trp Ala Arg
 305 310 315 320
 Ile Glu Asn Met Thr Ile Leu Gly Glu Asp Val His Val Ser Asp Glu
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 1 5 10
 cct tat cga acc aac tct tct ttc ggc tca aag tca tcg ctt ctc ttt 98
 Pro Tyr Arg Thr Asn Ser Ser Phe Gly Ser Lys Ser Ser Leu Leu Phe
 15 20 25 30
 cggtctcca tcc tcc tcc tcc tca gtc tct atg acg aca acg cgt gga 146
 Arg Ser Pro Ser Ser Ser Ser Val Ser Met Thr Thr Arg Gly
 35 40 45
 aac gtg gct gtg gcg gct gct aca tcc act gag gcg cta aga aaa 194
 Asn Val Ala Val Ala Ala Ala Thr Ser Thr Glu Ala Leu Arg Lys
 50 55 60

gga ata gcg gag ttc tac aat gaa act tcg ggt ttg tgg gaa gag att Gly Ile Ala Glu Phe Tyr Asn Glu Thr Ser Gly Leu Trp Glu Glu Ile	65	70	75	242
tgg gga gat cat atg cat cat ggc ttt tat gac cct gat tct tct gtt Trp Gly Asp His Met His His Gly Phe Tyr Asp Pro Asp Ser Ser Val	80	85	90	290
caa ctt tct gat tct ggt cac aag gaa gct cag atc cgt atg att gaa Gln Leu Ser Asp Ser Gly His Lys Glu Ala Gln Ile Arg Met Ile Glu	95	100	105	338
gag tct ctc cgt ttc gcc ggt gtt act gat gaa gag gag gag aaa aag Glu Ser Leu Arg Phe Ala Gly Val Thr Asp Glu Glu Glu Lys Lys	115	120	125	386
ata aag aaa gta gtg gat gtt ggg tgt ggg att gga gga agc tca aga Ile Lys Lys Val Val Asp Val Gly Cys Gly Ile Gly Gly Ser Ser Arg	130	135	140	434
tat ctt gcc tct aaa ttt gga gct gaa tgc att ggc att act ctc agc Tyr Leu Ala Ser Lys Phe Gly Ala Glu Cys Ile Gly Ile Thr Leu Ser	145	150	155	482
cct gtt cag gcc aag aga gcc aat gat ctc gcg gct gct caa tca ctc Pro Val Gln Ala Lys Arg Ala Asn Asp Leu Ala Ala Gln Ser Leu	160	165	170	530
tct cat aag gct tcc ttc caa gtt gcg gat gcg ttg gat cag cca ttc Ser His Lys Ala Ser Phe Gln Val Ala Asp Ala Leu Asp Gln Pro Phe	175	180	185	578
gaa gat gga aaa ttc gat cta gtg tgg tcg atg gag agt ggt gag cat Glu Asp Gly Lys Phe Asp Leu Val Trp Ser Met Glu Ser Gly Glu His	195	200	205	626
atg cct gac aag gcc aag ttt gta aaa gag ttg gta cgt gtg gcg gct Met Pro Asp Lys Ala Lys Phe Val Lys Glu Leu Val Arg Val Ala Ala	210	215	220	674
cca gga ggt agg ata ata ata gtg aca tgg tgc cat aga aat cta tct Pro Gly Gly Arg Ile Ile Ile Val Thr Trp Cys His Arg Asn Leu Ser	225	230	235	722
gcg ggg gag gaa gct ttg cag ccg tgg gag caa aac atc ttg gac aaa Ala Gly Glu Ala Leu Gln Pro Trp Glu Gln Asn Ile Leu Asp Lys	240	245	250	770
atc tgt aag acg ttc tat ctc ccg gct tgg tgc tcc acc gat gat tat Ile Cys Lys Thr Phe Tyr Leu Pro Ala Trp Cys Ser Thr Asp Asp Tyr	255	260	265	818
gtc aac ttg ctt caa tcc cat tct ctc cag gat att aag tgt gcg gat Val Asn Leu Leu Gln Ser His Ser Leu Gln Asp Ile Lys Cys Ala Asp	275	280	285	866

tgg tca gag aac gta gct cct ttc tgg cct gcg gtt ata cgg act gca	914
Trp Ser Glu Asn Val Ala Pro Phe Trp Pro Ala Val Ile Arg Thr Ala	
290	295
	300
tta aca tgg aag ggc ctt gtg tct ctg ctt cgt agt ggt atg aaa agt	962
Leu Thr Trp Lys Gly Leu Val Ser Leu Leu Arg Ser Gly Met Lys Ser	
305	310
	315
att aaa gga gca ttg aca atg cca ttg atg att gaa ggt tac aag aaa	1010
Ile Lys Gly Ala Leu Thr Met Pro Leu Met Ile Glu Gly Tyr Lys Lys	
320	325
	330
ggt gtc att aag ttt ggt atc atc act tgc cag aag cca ctc taa	1055
Gly Val Ile Lys Phe Gly Ile Ile Thr Cys Gln Lys Pro Leu	
335	340
	345
gtctaaagct atacta	1071
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	15
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20	25
	30
Pro Ser Ser Ser Ser Val Ser Met Thr Thr Thr Arg Gly Asn Val	
35	40
	45
Ala Val Ala Ala Ala Ala Thr Ser Thr Glu Ala Leu Arg Lys Gly Ile	
50	55
	60
Ala Glu Phe Tyr Asn Glu Thr Ser Gly Leu Trp Glu Glu Ile Trp Gly	
65	70
	75
	80
Asp His Met His His Gly Phe Tyr Asp Pro Asp Ser Ser Val Gln Leu	
85	90
	95
Ser Asp Ser Gly His Lys Glu Ala Gln Ile Arg Met Ile Glu Glu Ser	
100	105
	110
Leu Arg Phe Ala Gly Val Thr Asp Glu Glu Glu Lys Lys Ile Lys	
115	120
	125
Lys Val Val Asp Val Gly Cys Gly Ile Gly Ser Ser Arg Tyr Leu	
130	135
	140
Ala Ser Lys Phe Gly Ala Glu Cys Ile Gly Ile Thr Leu Ser Pro Val	
145	150
	155
	160
Gln Ala Lys Arg Ala Asn Asp Leu Ala Ala Gln Ser Leu Ser His	
165	170
	175

Lys Ala Ser Phe Gln Val Ala Asp Ala Leu Asp Gln Pro Phe Glu Asp
 180 185 190
 Gly Lys Phe Asp Leu Val Trp Ser Met Glu Ser Gly Glu His Met Pro
 195 200 205
 Asp Lys Ala Lys Phe Val Lys Glu Leu Val Arg Val Ala Ala Pro Gly
 210 215 220
 Gly Arg Ile Ile Ile Val Thr Trp Cys His Arg Asn Leu Ser Ala Gly
 225 230 235 240
 Glu Glu Ala Leu Gln Pro Trp Glu Gln Asn Ile Leu Asp Lys Ile Cys
 245 250 255
 Lys Thr Phe Tyr Leu Pro Ala Trp Cys Ser Thr Asp Asp Tyr Val Asn
 260 265 270
 Leu Leu Gln Ser His Ser Leu Gln Asp Ile Lys Cys Ala Asp Trp Ser
 275 280 285
 Glu Asn Val Ala Pro Phe Trp Pro Ala Val Ile Arg Thr Ala Leu Thr
 290 295 300
 Trp Lys Gly Leu Val Ser Leu Leu Arg Ser Gly Met Lys Ser Ile Lys
 305 310 315 320
 Gly Ala Leu Thr Met Pro Leu Met Ile Glu Gly Tyr Lys Lys Gly Val
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ctc gag atc gac gat gac cag aaa cta cgt gcg ttt tac gac aag aga 95
 Leu Glu Ile Asp Asp Gln Lys Leu Arg Ala Phe Tyr Asp Lys Arg
 20 25 30

atc tct caa gaa gtc agt gga gat gct ttg ggc gag gag ttc aaa gga 143
 Ile Ser Gln Glu Val Ser Gly Asp Ala Leu Gly Glu Glu Phe Lys Gly
 35 40 45

tac gtt ttc aag atc aag ggt ggt tgc gat aag caa ggt ttc cca atg Tyr Val Phe Lys Ile Lys Gly Gly Cys Asp Lys Gln Gly Phe Pro Met	50	55	60	191
aag cag gga gtt ttg act cca ggc cgt gtt cgc ctt ttg ctt cac cga Lys Gln Gly Val Leu Thr Pro Gly Arg Val Arg Leu Leu His Arg	65	70	75	239
gga act cct tgc ttc aga gga cat gga agg aga act ggt gag agg aga Gly Thr Pro Cys Phe Arg Gly His Gly Arg Arg Thr Gly Glu Arg Arg	80	85	90	287
aga aag tct gtt cgt ggt tgc att gtg agc cct gat ctc tct gtt ctg Arg Lys Ser Val Arg Gly Cys Ile Val Ser Pro Asp Leu Ser Val Leu	100	105	110	335
aac ctt gtc att gtg aag aag ggt gag aac gat ctt cct ggg ctt acc Asn Leu Val Ile Val Lys Lys Gly Glu Asn Asp Leu Pro Gly Leu Thr	115	120	125	383
gat cat gag agc aag atg aga gga cca aag aga gcc tcc aag atc cgt Asp His Glu Ser Lys Met Arg Gly Pro Lys Arg Ala Ser Lys Ile Arg	130	135	140	431
aaa ctg ttt aac ctc aag aag gaa gat gat gtc agg acc tat gtc aac Lys Leu Phe Asn Leu Lys Lys Glu Asp Asp Val Arg Thr Tyr Val Asn	145	150	155	479
act tac cgc cgc aag ttc aca aac aag ggc aag gaa gtt agc aaa Thr Tyr Arg Arg Lys Phe Thr Asn Lys Lys Gly Lys Glu Val Ser Lys	160	165	170	527
gcc cct aag atc cag agg ctt gtg acc cca ttg act ctt cag agg aag Ala Pro Lys Ile Gln Arg Leu Val Thr Pro Leu Thr Leu Gln Arg Lys	180	185	190	575
aga gct aga att gct gac aag aag aaa att gct aag gct aat tct Arg Ala Arg Ile Ala Asp Lys Lys Lys Ile Ala Lys Ala Asn Ser	195	200	205	623
gat gct gct gat tac cag aag ctt ctc gcc tcg agg ttg aag gaa cag Asp Ala Ala Asp Tyr Gln Lys Leu Leu Ala Ser Arg Leu Lys Glu Gln	210	215	220	671
cgt gac agg agg agt gag agt ttg gca aaa gag agg tcg aga ctc tct Arg Asp Arg Arg Ser Glu Ser Leu Ala Lys Glu Arg Ser Arg Leu Ser	225	230	235	719
tct gct gct gcc aag ccc tct gtc aca gct taa aaaagcttga gattca Ser Ala Ala Ala Lys Pro Ser Val Thr Ala	240	245	250	768

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<212> PRT

<213> *Arabidopsis thaliana*

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					20			25				30			

Ser	Gln	Glu	Val	Ser	Gly	Asp	Ala	Leu	Gly	Glu	Gly	Phe	Lys	Gly	Tyr
					35			40			45				

Val	Phe	Lys	Ile	Lys	Gly	Gly	Cys	Asp	Lys	Gln	Gly	Phe	Pro	Met	Lys
					50			55			60				

Gln	Gly	Val	Leu	Thr	Pro	Gly	Arg	Val	Arg	Leu	Leu	Leu	His	Arg	Gly
					65			70		75			80		

Thr	Pro	Cys	Phe	Arg	Gly	His	Gly	Arg	Arg	Thr	Gly	Glu	Arg	Arg	Arg
					85			90				95			

Lys	Ser	Val	Arg	Gly	Cys	Ile	Val	Ser	Pro	Asp	Leu	Ser	Val	Leu	Asn
						100		105				110			

Leu	Val	Ile	Val	Lys	Lys	Gly	Glu	Asn	Asp	Leu	Pro	Gly	Leu	Thr	Asp
					115			120				125			

His	Glu	Ser	Lys	Met	Arg	Gly	Pro	Lys	Arg	Ala	Ser	Lys	Ile	Arg	Lys
					130			135			140				

Leu	Phe	Asn	Leu	Lys	Lys	Glu	Asp	Asp	Val	Arg	Thr	Tyr	Val	Asn	Thr
					145			150		155			160		

Tyr	Arg	Arg	Lys	Phe	Thr	Asn	Lys	Lys	Gly	Lys	Glu	Val	Ser	Lys	Ala
					165			170			175				

Pro	Lys	Ile	Gln	Arg	Leu	Val	Thr	Pro	Leu	Thr	Leu	Gln	Arg	Lys	Arg
					180			185			190				

Ala	Arg	Ile	Ala	Asp	Lys	Lys	Lys	Ile	Ala	Lys	Ala	Asn	Ser	Asp
					195			200			205			

Ala	Ala	Asp	Tyr	Gln	Lys	Leu	Leu	Ala	Ser	Arg	Leu	Lys	Glu	Gln	Arg
					210			215			220				

Asp	Arg	Arg	Ser	Glu	Ser	Leu	Ala	Lys	Glu	Arg	Ser	Arg	Leu	Ser	Ser
					225			230		235		240			

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<212> DNA

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ctttctctt ttctctgtca ctaattttca g act gag aaa gct ttt ctt aag 167
Thr Glu Lys Ala Phe Leu Lys
5 10

cag cct aag gtc ttc ctt ag gtaatttgat gattcgattt ctctctgttc 217
Gln Pro Lys Val Phe Leu Se
15

tctattgttt cattgtatTTT aagtccaaag ttgtttatATG tgttcattGTG ttctgattTA 277
tcaag c tcg aag aaa tct gga aag gga aag aga cct gga aaa ggt gga 325
r Ser Lys Lys Ser Gly Lys Gly Lys Arg Pro Gly Lys Gly Gly
20 25 30

aac cgt ttc tgg aag aac att ggt ttg ggc ttc aag act cct cgt gaa 373
Asn Arg Phe Trp Lys Asn Ile Gly Leu Gly Phe Lys Thr Pro Arg Glu
35 40 45

gcc att gat g gtagtttAA gctttAAact cgTTATAATA gataaggAAC 423
Ala Ile Asp G
50

tctggatttG tgTTGTTcat atagtcgata gatttcaaAT gCTATTGTTG tttGAGAAT 483
cttaagcttt ggTTTAgTGA gttctgattc ttcaGTTTA tctggatcta cattactgtt 543

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 gttattgtgt atttgtgtgg aacag ga gct tac gac aag aaa tgc ccc 714
 ly Ala Tyr Val Asp Lys Lys Cys Pro
 55 60
 ttc act gga act gtt tcc att aga ggt cgt atc tta gct ggt act tgc 762
 Phe Thr Gly Thr Val Ser Ile Arg Gly Arg Ile Leu Ala Gly Thr Cys
 65 70 75
 cac agt gcg aaa atg cag agg acc att atc gtg cga agg gat tac ctt 810
 His Ser Ala Lys Met Gln Arg Thr Ile Ile Val Arg Arg Asp Tyr Leu
 80 85 90
 cac ttt gtg aag aag tat cag ag gtaaaattcat acattctcat acttcttcc 863
 His Phe Val Lys Lys Tyr Gln Ar
 95
 atagagtctt acacattgat gtttaagaaa gtaatatcct ttttgttctt ag g tat 919
 9 Tyr
 100
 gag aag agg cat tca aac att ccg gct cat gtc tca cca tgc ttc cgt 967
 Glu Lys Arg His Ser Asn Ile Pro Ala His Val Ser Pro Cys Phe Arg
 105 110 115
 gtt aag gaa gga gac cat atc atc att ggc caa tgc ag gttatgatct 1015
 Val Lys Glu Gly Asp His Ile Ile Ile Gly Gln Cys Ar
 120 125
 gattcaaacc tacaaattgt ctccattgat tctgattatc gtgaatttgt tttgatcttt 1075
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 g Pro Leu Ser Lys Thr Val Arg Phe
 130 135
 aat gtg ttg aag gtg ata cca gct ggg tct tct tct tca ttt gga aag 1175
 Asn Val Leu Lys Val Ile Pro Ala Gly Ser Ser Ser Phe Gly Lys
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 <212> PRT
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Phe Leu Ser Ser Lys Ser Gly Lys Gly Lys Arg Pro Gly Lys Gly
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 35 40 45

Glu Ala Ile Asp Gly Ala Tyr Val Asp Lys Lys Cys Pro Phe Thr Gly
 50 55 60

Thr Val Ser Ile Arg Gly Arg Ile Leu Ala Gly Thr Cys His Ser Ala
 65 70 75 8

Lys Met Gln Arg Thr Ile Ile Val Arg Arg Asp Tyr Leu His Phe Val
 85 90 95

Lys Lys Tyr Gln Arg Tyr Glu Lys Arg His Ser Asn Ile Pro Ala His
 100 105 110

Val Ser Pro Cys Phe Arg Val Lys Glu Gly Asp His Ile Ile Ile Gly
 115 120 125

Gln Cys Arg Pro Leu Ser Lys Thr Val Arg Phe Asn Val Leu Lys Val
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Ile Pro Ala Gly Ser Ser Ser Phe Gly Lys Lys Ala Phe Thr Gly
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<210> 31
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 <212> DNA
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 1 5 10

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 Leu Ile Glu Glu Gly Leu Ile Leu Gln Glu Val Lys Leu Tyr Ala Glu
 15 20 25

gat ggt tca gtg gac ttt aat gga aac cca cca ttg aag gag aaa aca 148
 Asp Gly Ser Val Asp Phe Asn Gly Asn Pro Pro Leu Lys Glu Lys Thr
 30 35 40

gga aac tgg aaa gct tgt cct ttt att ctt ggt aat gaa tgt tgt gag 196
 Gly Asn Trp Lys Ala Cys Pro Phe Ile Leu Gly Asn Glu Cys Cys Glu
 45 50 55

agg cta gct tac tat ggt att gct ggg aat tta atc act tac ctc acc		244	
Arg Leu Ala Tyr Tyr Gly Ile Ala Gly Asn Leu Ile Thr Tyr Leu Thr			
60	65	70	
act aag ctt cac caa gga aat gtt tct gct gct aca aac gtt acc aca		292	
Thr Lys Leu His Gln Gly Asn Val Ser Ala Ala Thr Asn Val Thr Thr			
75	80	85	90
tgg caa ggg act tgt tat ctc act cct ctc att gga gct gtt ctg gct		340	
Trp Gln Gly Thr Cys Tyr Leu Thr Pro Leu Ile Gly Ala Val Leu Ala			
95	100	105	
gat gct tac tgg gga cgt tac tgg acc atc gct tgt ttc tcc ggg att		388	
Asp Ala Tyr Trp Gly Arg Tyr Trp Thr Ile Ala Cys Phe Ser Gly Ile			
110	115	120	
tat ttc atc ggg atg tct gcg tta act ctt tca gct tca gtt ccg gca		436	
Tyr Phe Ile Gly Met Ser Ala Leu Thr Leu Ser Ala Ser Val Pro Ala			
125	130	135	
ttg aag cca gcg gaa tgt att ggt gac ttt tgt cca tct gca acg cca		484	
Leu Lys Pro Ala Glu Cys Ile Gly Asp Phe Cys Pro Ser Ala Thr Pro			
140	145	150	
gct cag tat gcg atg ttc ttt ggt ggg ctt tac ctg atc gct ctt gga		532	
Ala Gln Tyr Ala Met Phe Phe Gly Gly Leu Tyr Leu Ile Ala Leu Gly			
155	160	165	170
act gga ggt atc aaa ccg tgt gtc tca tcc ttc ggt gcc gat cag ttt		580	
Thr Gly Gly Ile Lys Pro Cys Val Ser Ser Phe Gly Ala Asp Gln Phe			
175	180	185	
gat gac acg gac tct cgg gaa cga gtt aga aaa gct tcg ttc ttt aac		628	
Asp Asp Thr Asp Ser Arg Glu Arg Val Arg Lys Ala Ser Phe Phe Asn			
190	195	200	
tgg ttt tac ttc tcc atc aat att gga gca ctt gtg tca tct agt ctt		676	
Trp Phe Tyr Phe Ser Ile Asn Ile Gly Ala Leu Val Ser Ser Ser Leu			
205	210	215	
cta gtt tgg att caa gag aat cgg ggg tgg ggt tta ggg ttt ggg ata		724	
Leu Val Trp Ile Gln Glu Asn Arg Gly Trp Gly Leu Gly Phe Gly Ile			
220	225	230	
cca aca gtg ttc atg gga cta gcc att gca agt ttc ttc ttt ggc aca		772	
Pro Thr Val Phe Met Gly Leu Ala Ile Ala Ser Phe Phe Phe Gly Thr			
235	240	245	250
cct ctt tat agg ttt cag aaa cct gga gga agc cct ata act cgg att		820	
Pro Leu Tyr Arg Phe Gln Lys Pro Gly Gly Ser Pro Ile Thr Arg Ile			
255	260	265	
tcc caa gtc gtg gtt gct tcg ttc cgg aaa tcg tct gtc aaa gtc cct		868	
Ser Gln Val Val Val Ala Ser Phe Arg Lys Ser Ser Val Lys Val Pro			
270	275	280	
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Glu Asp Ala Thr Leu Leu Tyr Glu Thr Gln Asp Lys Asn Ser Ala Ile			
285	290	295	
gct gga agt aga aaa atc gag cat acc gat gat tgc cag tat ctt gac			
Ala Gly Ser Arg Lys Ile Glu His Thr Asp Asp Cys Gln Tyr Leu Asp			964
300	305	310	
aaa gcc gct gtt atc tca gaa gaa gaa tcg aaa tcc gga gat tat tcc			
Lys Ala Ala Val Ile Ser Glu Glu Ser Lys Ser Gly Asp Tyr Ser			1012
315	320	325	330
aac tcg tgg aga cta tgc acg gtt acg caa gtc gaa gaa ctc aag att			
Asn Ser Trp Arg Leu Cys Thr Val Thr Gln Val Glu Glu Leu Lys Ile			1060
335	340	345	
ctg atc cga atg ttc cca atc tgg gct tct ggt atc att ttc tca gct			
Leu Ile Arg Met Phe Pro Ile Trp Ala Ser Gly Ile Ile Phe Ser Ala			1108
350	355	360	
gta tac gca caa atg tcc aca atg ttt gtt caa caa ggc cga gcc atg			
Val Tyr Ala Gln Met Ser Thr Met Phe Val Gln Gln Gly Arg Ala Met			1156
365	370	375	
aac tgc aaa att gga tca ttc cag ctt cct gca gca ctc ggg aca			
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380	385	390	
ttc gac aca gca agc gtc atc atc tgg gtg ccg ctc tac gac cgg ttc			
Phe Asp Thr Ala Ser Val Ile Ile Trp Val Pro Leu Tyr Asp Arg Phe			1252
395	400	405	410
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Ile Val Pro Leu Ala Arg Lys Phe Thr Gly Val Asp Lys Gly Phe Thr			1300
415	420	425	
gag ata caa aga atg gga att ggt ctg ttt gtc tct gtt ctc tgt atg			
Glu Ile Gln Arg Met Gly Ile Gly Leu Phe Val Ser Val Leu Cys Met			1348
430	435	440	
gca gct gca gct atc gtc gaa atc atc cgt ctc cat atg gcc aac gat			
Ala Ala Ala Ala Ile Val Glu Ile Ile Arg Leu His Met Ala Asn Asp			1396
445	450	455	
ctt gga tta gtc gag tca gga gcc cca gtt ccc ata tcc gtc ttg tgg			
Leu Gly Leu Val Glu Ser Gly Ala Pro Val Pro Ile Ser Val Leu Trp			1444
460	465	470	
cag att cca cag tac ttc att ctc ggt gca gcc gaa gta ttc tac ttc			
Gln Ile Pro Gln Tyr Phe Ile Leu Gly Ala Ala Glu Val Phe Tyr Phe			1492
475	480	485	490
atc ggt cag ctc gag ttc ttc tac gac caa tct cca gat gca atg aga			
Ile Gly Gln Leu Glu Phe Phe Tyr Asp Gln Ser Pro Asp Ala Met Arg			1540
495	500	505	
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Ser Leu Cys Ser Ala Leu Ala Leu Leu Thr Asn Ala Leu Gly Asn Tyr			1588

510	515	520	
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ggg caa gaa ggt tgg att tcg gat aat ctc aat tca ggt cat ctc gat Gly Gln Glu Gly Trp Ile Ser Asp Asn Leu Asn Ser Gly His Leu Asp 540	545	550	1684
tac ttc ttc tgg ctc ttg gct ggt ctt agc ctt gtg aac atg gcg gtt Tyr Phe Phe Trp Leu Leu Ala Gly Leu Ser Leu Val Asn Met Ala Val 555	560	565	1732
tac ttc ttc tct gct gct agg tat aag caa aag aaa gct tcg tcg tag Tyr Phe Phe Ser Ala Ala Arg Tyr Lys Gln Lys Lys Ala Ser Ser 575	580	585	1780
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Pro Phe Ile Leu Gly Asn Glu Cys Cys Glu Arg Leu Ala Tyr Tyr Gly 50	55	60	
Ile Ala Gly Asn Leu Ile Thr Tyr Leu Thr Thr Lys Leu His Gln Gly 65	70	75	80
Asn Val Ser Ala Ala Thr Asn Val Thr Thr Trp Gln Gly Thr Cys Tyr 85	90		95
Leu Thr Pro Leu Ile Gly Ala Val Leu Ala Asp Ala Tyr Trp Gly Arg 100	105		110
Tyr Trp Thr Ile Ala Cys Phe Ser Gly Ile Tyr Phe Ile Gly Met Ser 115	120	125	
Ala Leu Thr Leu Ser Ala Ser Val Pro Ala Leu Lys Pro Ala Glu Cys 130	135	140	
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Phe Gly Gly Leu Tyr Leu Ile Ala Leu Gly Thr Gly Gly Ile Lys Pro
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 Cys Val Ser Ser Phe Gly Ala Asp Gln Phe Asp Asp Thr Asp Ser Arg
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 Glu Arg Val Arg Lys Ala Ser Phe Phe Asn Trp Phe Tyr Phe Ser Ile
 195 200 205
 Asn Ile Gly Ala Leu Val Ser Ser Ser Leu Leu Val Trp Ile Gln Glu
 210 215 220
 Asn Arg Gly Trp Gly Leu Gly Phe Gly Ile Pro Thr Val Phe Met Gly
 225 230 235 240
 Leu Ala Ile Ala Ser Phe Phe Phe Gly Thr Pro Leu Tyr Arg Phe Gln
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 Lys Pro Gly Gly Ser Pro Ile Thr Arg Ile Ser Gln Val Val Val Ala
 260 265 270
 Ser Phe Arg Lys Ser Ser Val Lys Val Pro Glu Asp Ala Thr Leu Leu
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 Glu His Thr Asp Asp Cys Gln Tyr Leu Asp Lys Ala Ala Val Ile Ser
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 Ile Trp Ala Ser Gly Ile Ile Phe Ser Ala Val Tyr Ala Gln Met Ser
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 Phe Gln Leu Pro Pro Ala Ala Leu Gly Thr Phe Asp Thr Ala Ser Val
 385 390 395 400
 Ile Ile Trp Val Pro Leu Tyr Asp Arg Phe Ile Val Pro Leu Ala Arg
 405 410 415
 Lys Phe Thr Gly Val Asp Lys Gly Phe Thr Glu Ile Gln Arg Met Gly
 420 425 430
 Ile Gly Leu Phe Val Ser Val Leu Cys Met Ala Ala Ala Ile Val
 435 440 445
 Glu Ile Ile Arg Leu His Met Ala Asn Asp Leu Gly Leu Val Glu Ser
 450 455 460

Gly Ala Pro Val Pro Ile Ser Val Leu Trp Gln Ile Pro Gln Tyr Phe
 465 470 475 480

Ile Leu Gly Ala Ala Glu Val Phe Tyr Phe Ile Gly Gln Leu Glu Phe
 485 490 495

Phe Tyr Asp Gln Ser Pro Asp Ala Met Arg Ser Leu Cys Ser Ala Leu
 500 505 510

Ala Leu Leu Thr Asn Ala Leu Gly Asn Tyr Leu Ser Ser Leu Ile Leu
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Thr Leu Val Thr Tyr Phe Thr Thr Arg Asn Gly Gln Glu Gly Trp Ile
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Ser Asp Asn Leu Asn Ser Gly His Leu Asp Tyr Phe Phe Trp Leu Leu
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Leu Val Phe Arg Ser Ser Leu Ala Gly Asp Asp Gly Thr Ser Gly Gly
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ggt ctt agc gga ttc gtc ggg aag att aac tct agt atc cgt agc tct 148
Gly Leu Ser Gly Phe Val Gly Lys Ile Asn Ser Ser Ile Arg Ser Ser
30 35 40

cga att ggg ctc ttt tct aag ccg cct cca ggg ctt cct gct cct aga 196
Arg Ile Gly Leu Phe Ser Lys Pro Pro Pro Gly Leu Pro Ala Pro Arg
45 50 55

aaa gaa gaa gcg ccg tcg att cgg tgg agg aaa ggg gaa tta atc ggt 244
Lys Glu Glu Ala Pro Ser Ile Arg Trp Arg Lys Gly Glu Leu Ile Gly
60 65 70 75

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Cys Gly Ala Phe Gly Arg Val Tyr Met Gly Met Asn Leu Asp Ser Gly			
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Glu Leu Leu Ala Ile Lys Gln Val Leu Ile Ala Pro Ser Ser Ala Ser			
95	100	105	
aag gag aag act cag ggt cac atc cga gag ctt gag gaa gaa gta caa	388		
Lys Glu Lys Thr Gln Gly His Ile Arg Glu Leu Glu Glu Val Gln			
110	115	120	
ctt ctt aag aat ctt tca cat ccg aac atc gtt aga tac ttg ggt act	436		
Leu Leu Lys Asn Leu Ser His Pro Asn Ile Val Arg Tyr Leu Gly Thr			
125	130	135	
gta aga gag agt gat tcg ttg aat att ttg atg gag ttt gtt cct ggt	484		
Val Arg Glu Ser Asp Ser Leu Asn Ile Leu Met Glu Phe Val Pro Gly			
140	145	150	155
gga tca ata tca tct ttg ttg gag aag ttt gga tct ttt cct gag cct	532		
Gly Ser Ile Ser Ser Leu Leu Glu Lys Phe Gly Ser Phe Pro Glu Pro			
160	165	170	
gtg att att atg tac aca aag caa ctt ctg ctt ggg ctg gaa tat ctt	580		
Val Ile Ile Met Tyr Thr Lys Gln Leu Leu Leu Gly Leu Glu Tyr Leu			
175	180	185	
cac aac aat ggg atc atg cat cga gat att aag ggg gca aat att ttg	628		
His Asn Asn Gly Ile Met His Arg Asp Ile Lys Gly Ala Asn Ile Leu			
190	195	200	
gtc gat aac aaa ggt tgc atc aga ctc gca gat ttt ggt gct tcc aag	676		
Val Asp Asn Lys Gly Cys Ile Arg Leu Ala Asp Phe Gly Ala Ser Lys			
205	210	215	
aaa gtt gta gag cta gct act gta aat ggt gcc aaa tct atg aag ggg	724		
Lys Val Val Glu Leu Ala Thr Val Asn Gly Ala Lys Ser Met Lys Gly			
220	225	230	235
acg cct tat tgg atg gct cct gaa gtc att ctc cag act ggt cat agc	772		
Thr Pro Tyr Trp Met Ala Pro Glu Val Ile Leu Gln Thr Gly His Ser			
240	245	250	
ttc tct gct gat ata tgg agt gtt ggg tgc act gtg att gag atg gct	820		
Phe Ser Ala Asp Ile Trp Ser Val Gly Cys Thr Val Ile Glu Met Ala			
255	260	265	
acg ggg aag cct ccc tgg agc gag cag tat cag cag ttt gct gct gtc	868		
Thr Gly Lys Pro Pro Trp Ser Glu Gln Tyr Gln Gln Phe Ala Ala Val			
270	275	280	
ctt cat att ggt aga aca aaa gct cat cct cca att cca gaa gac ctc	916		
Leu His Ile Gly Arg Thr Lys Ala His Pro Pro Ile Pro Glu Asp Leu			
285	290	295	
tca cca gag gct aaa gac ttt cta atg aaa tgc tta cac aaa gaa cca	964		
Ser Pro Glu Ala Lys Asp Phe Leu Met Lys Cys Leu His Lys Glu Pro			

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agc ttg aga ctc tct gca acc gaa ttg ctt cag cac ccg ttt gtc act Ser Leu Arg Leu Ser Ala Thr Glu Leu Leu Gln His Pro Phe Val Thr				1012
320	325	330		
gga aag cgc cag gaa cct tat cca gct tac cgt aat tct ctt acg gaa Gly Lys Arg Gln Glu Pro Tyr Pro Ala Tyr Arg Asn Ser Leu Thr Glu				1060
335	340	345		
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350	355	360		
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365	370	375		
gaa ctg gga agc ttg agg agt tcc att ata tac cca cag aag tca aat Glu Leu Gly Ser Leu Arg Ser Ser Ile Ile Tyr Pro Gln Lys Ser Asn				1204
380	385	390	395	
aac tca gga ttt ggt tgg cga gat gga gac tct gat gac ctt tgt cag Asn Ser Gly Phe Gly Trp Arg Asp Gly Asp Ser Asp Asp Leu Cys Gln				1252
400	405	410		
acc gat atg gat gat ctc tgc aac att gaa tca gtc aga aac aat gtt Thr Asp Met Asp Asp Leu Cys Asn Ile Glu Ser Val Arg Asn Asn Val				1300
415	420	425		
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430	435	440		
tcc acg gat aac tgg tct tgc aag ttt gat gaa agc cca aaa gtg atg Ser Thr Asp Asn Trp Ser Cys Lys Phe Asp Glu Ser Pro Lys Val Met				1396
445	450	455		
aaa agc aaa tct aac ctg ctt tct tac caa gct tct caa ctc caa act Lys Ser Lys Ser Asn Leu Leu Ser Tyr Gln Ala Ser Gln Leu Gln Thr				1444
460	465	470	475	
gga gtt cca tgt gat gag gaa acc agc tta aca ttt gct ggt ggc tct Gly Val Pro Cys Asp Glu Glu Thr Ser Leu Thr Phe Ala Gly Gly Ser				1492
480	485	490		
tcc gtt gca gag gat tat aaa ggc aca gag ttg aaa ata aaa tca Ser Val Ala Glu Asp Asp Tyr Lys Gly Thr Glu Leu Lys Ile Lys Ser				1540
495	500	505		
ttt ttg gat gag aag gct cag gat ttg aaa agg ttg cag acc cct ctg Phe Leu Asp Glu Lys Ala Gln Asp Leu Lys Arg Leu Gln Thr Pro Leu				1588
510	515	520		
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525	530	535		

ctt gga gac acc aat atc tac aat tta cca aac tta cca agt ata agc Leu Gly Asp Thr Asn Ile Tyr Asn Leu Pro Asn Leu Pro Ser Ile Ser 540 545 550 555	1684
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aga gtg atg cag tca gga act gaa cca act caa gtc aac gag tcg acc Arg Val Met Gln Ser Gly Thr Glu Pro Thr Gln Val Asn Glu Ser Thr 590 595 600	1828
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cga cac gct ggt gca gga ggg aag act cca tta tca ggc cac aaa gga Arg His Ala Gly Ala Gly Lys Thr Pro Leu Ser Gly His Lys Gly 640 645 650	1972
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35 40 45

Ser Lys Pro Pro Pro Gly Leu Pro Ala Pro Arg Lys Glu Glu Ala Pro
50 55 60

Ser Ile Arg Trp Arg Lys Gly Glu Leu Ile Gly Cys Gly Ala Phe Gly
65 70 75 80

Arg Val Tyr Met Gly Met Asn Leu Asp Ser Gly Glu Leu Leu Ala Ile
85 90 95

Lys Gln Val Leu Ile Ala Pro Ser Ser Ala Ser Lys Glu Lys Thr Gln
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 Gly His Ile Arg Glu Leu Glu Glu Val Gln Leu Leu Lys Asn Leu
 115 120 125
 Ser His Pro Asn Ile Val Arg Tyr Leu Gly Thr Val Arg Glu Ser Asp
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 Ser Leu Asn Ile Leu Met Glu Phe Val Pro Gly Gly Ser Ile Ser Ser
 145 150 155 160
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 165 170 175
 Thr Lys Gln Leu Leu Leu Gly Leu Glu Tyr Leu His Asn Asn Gly Ile
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 Met His Arg Asp Ile Lys Gly Ala Asn Ile Leu Val Asp Asn Lys Gly
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 Cys Ile Arg Leu Ala Asp Phe Gly Ala Ser Lys Lys Val Val Glu Leu
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 Ala Thr Val Asn Gly Ala Lys Ser Met Lys Gly Thr Pro Tyr Trp Met
 225 230 235 240
 Ala Pro Glu Val Ile Leu Gln Thr Gly His Ser Phe Ser Ala Asp Ile
 245 250 255
 Trp Ser Val Gly Cys Thr Val Ile Glu Met Ala Thr Gly Lys Pro Pro
 260 265 270
 Trp Ser Glu Gln Tyr Gln Gln Phe Ala Ala Val Leu His Ile Gly Arg
 275 280 285
 Thr Lys Ala His Pro Pro Ile Pro Glu Asp Leu Ser Pro Glu Ala Lys
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 Ala Thr Glu Leu Leu Gln His Pro Phe Val Thr Gly Lys Arg Gln Glu
 325 330 335
 Pro Tyr Pro Ala Tyr Arg Asn Ser Leu Thr Glu Cys Gly Asn Pro Ile
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 355 360 365
 Arg Ser Thr Cys Ser Gly Leu Lys Asp Val Cys Glu Leu Gly Ser Leu
 370 375 380
 Arg Ser Ser Ile Ile Tyr Pro Gln Lys Ser Asn Asn Ser Gly Phe Gly
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 Asp Tyr Lys Gly Thr Glu Leu Lys Ile Lys Ser Phe Leu Asp Glu Lys
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 565 570 575
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 580 585 590
 Gly Thr Glu Pro Thr Gln Val Asn Glu Ser Thr Lys Lys Gly Val Asn
 595 600 605
 Asn Ser Arg Cys Phe Ser Glu Ile Arg Arg Lys Trp Glu Glu Glu Leu
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Gly Thr Gly Ser Pro Pro Pro Pro Pro Pro Pro Ala Arg Trp					
20 25 30					
agg gta gcg ggg gag gga gga ttg gat aca aca cca ccg ccg ccc cct					144
Arg Val Ala Gly Glu Gly Gly Leu Asp Thr Thr Pro Pro Pro Pro Pro					
35 40 45					
cca acg gca gat aca gtc gtg gcg gga agg acg agt tta ggt gag gcg					192
Pro Thr Ala Asp Thr Val Val Ala Gly Arg Thr Ser Leu Gly Glu Ala					
50 55 60					
ccc cct cct cgt cag cct cca cgt cct cca aca gca ccg tgg tca gcg					240
Pro Pro Pro Arg Gln Pro Pro Arg Pro Pro Thr Ala Arg Trp Ser Ala					
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Met Gly Arg Val Met Cys Ser Pro Pro Ile Pro Leu Ser Arg Ser Arg					
85 90 95					
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Leu Ala Leu Asp Asp Gln Arg Trp Pro Asp Trp Thr Thr Asn Gly Trp					
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Leu Ser Met Arg Pro Thr Ser Ser Pro Thr Arg Arg Ile Asp Pro Gln					
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Gly Ala Arg Arg Ser Ser Val Ser Pro Ala Pro Val Thr Thr Gly Met					
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Lys Asp Tyr Lys Glu Gly Gly Ile Ala Ala Tyr Phe Gly Leu Arg Val					
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Leu Arg Cys Tyr Ser Arg Ile Val Arg Ser Met Lys Arg Pro Gly Asn					
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cca agc atg acc tac cta aca tgc ggg ctg gga tgg atg acc gtc gtc Pro Ser Met Thr Tyr Leu Thr Cys Gly Leu Gly Trp Met Thr Val Val 275 280 285			864
gta ctg ccg gcg ata gtg gtc cac tgt tat atg cgc cga cat acg gaa Val Leu Pro Ala Ile Val Val His Cys Tyr Met Arg Arg His Thr Glu 290 295 300			912
ggg gga tgg cgg tat gcg gca ctc gag gag cat aag acg gag ccg gga Gly Gly Trp Arg Tyr Ala Ala Leu Glu Glu His Lys Thr Glu Pro Gly 305 310 315 320			960
cga aat gaa aag atc acc cgg agt aga cgc aac tcg gcg ttc ggc ggg Arg Asn Glu Lys Ile Thr Arg Ser Arg Arg Asn Ser Ala Phe Gly Gly 325 330 335			1008
ctg gtc ggt cga aat aaa aga cga aag aag tcc aag gtc tcc ggg gca Leu Val Gly Arg Asn Lys Arg Arg Lys Ser Lys Val Ser Gly Ala 340 345 350			1056
ccg aca gcg gtt tac aca gcg atg ttt ttc atg ttc tcc acg gca atc Pro Thr Ala Val Tyr Thr Ala Met Phe Phe Met Phe Ser Thr Ala Ile 355 360 365			1104
aag ggg atg gtg gtg tgc aca atg aaa aaa aaa gtc aaa aaa agt gcg Lys Gly Met Val Val Cys Thr Met Lys Lys Val Lys Lys Ser Ala 370 375 380			1152
aat cgc aga ctc cgc cag ttg ctc cga tgg gcg cga tac cac gcg aac Asn Arg Arg Leu Arg Gln Leu Leu Arg Trp Ala Arg Tyr His Ala Asn 385 390 395 400			1200
gcg ttc ttg ctc tgt tct ctt gca tgc gca cga ttc gcg gca tcg cga Ala Phe Leu Leu Cys Ser Leu Ala Cys Ala Arg Phe Ala Ala Ser Arg 405 410 415			1248
acg gtc atc cat tgc agt att tac cca cgt ttc ggc ccc tta gcc acg Thr Val Ile His Cys Ser Ile Tyr Pro Arg Phe Gly Pro Leu Ala Thr 420 425 430			1296
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Glu Ala Asp Thr Thr Arg His Glu Asn Asp Asp Ala Arg Lys Val Met			
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Glu Asp Met Ala Lys Arg Met Asp Asp Ser Ser Ser Gly Ser Thr Leu			
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agc acg ctc acg act gac gag acg tac cac acc acc acg gag gtg acc		1488	
Ser Thr Leu Thr Asp Glu Thr Tyr His Thr Thr Glu Val Thr			
485	490	495	
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Asp Phe Asp Ser Ser Pro Ser Trp Gly Arg Cys Ser Ser Arg Arg Pro			
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Pro Ala Leu Leu Glu Ser Thr Phe Arg Arg Ser Pro Arg Gly Ser Thr			
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Pro Thr Ala Asp Thr Val Val Ala Gly Arg Thr Ser Leu Gly Glu Ala			
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Pro Pro Pro Arg Gln Pro Pro Arg Pro Pro Thr Ala Arg Trp Ser Ala			
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Met Gly Arg Val Met Cys Ser Pro Pro Ile Pro Leu Ser Arg Ser Arg			
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Leu Ala Leu Asp Asp Gln Arg Trp Pro Asp Trp Thr Thr Asn Gly Trp			
100	105	110	

Leu Ser Met Arg Pro Thr Ser Ser Pro Thr Arg Arg Ile Asp Pro Gln
115 120 125

Gly Ala Arg Arg Ser Ser Val Ser Pro Ala Pro Val Thr Thr Gly Met
130 135 140

Ala Thr Ser Arg Thr Asp Asp Thr Leu Ile Glu Ala Glu Thr Gly Arg
145 150 155 160

Asp Trp Thr Arg Lys Arg Met Val Arg Lys Leu Leu Lys Ala Arg Ala
165 170 175

Lys Asp Tyr Lys Glu Gly Gly Ile Ala Ala Tyr Phe Gly Leu Arg Val
180 185 190

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Leu Lys Phe Thr Cys Arg Arg Asp Val Ala Ile Ala Thr Phe Ser Gly
210 215 220

Thr Gly Arg Met Gln Leu Ser Met Asn Ser Arg Leu Arg Val Glu Ser
225 230 235 240

Leu Val Ser Ala Gly Gln Ser Val Ala Ser Phe Cys Leu Phe Leu Ile
245 250 255

Cys Thr Ala Pro Ser Ala Met Arg Leu Val Ser Leu Leu Thr Leu Thr
260 265 270

Pro Ser Met Thr Tyr Leu Thr Cys Gly Leu Gly Trp Met Thr Val Val
275 280 285

Val Leu Pro Ala Ile Val Val His Cys Tyr Met Arg Arg His Thr Glu
290 295 300

Gly Gly Trp Arg Tyr Ala Ala Leu Glu Glu His Lys Thr Glu Pro Gly
305 310 315 320

Arg Asn Glu Lys Ile Thr Arg Ser Arg Arg Asn Ser Ala Phe Gly Gly
325 330 335

Leu Val Gly Arg Asn Lys Arg Arg Lys Lys Ser Lys Val Ser Gly Ala
340 345 350

Pro Thr Ala Val Tyr Thr Ala Met Phe Phe Met Phe Ser Thr Ala Ile
355 360 365

Lys Gly Met Val Val Cys Thr Met Lys Lys Lys Val Lys Ser Ala
370 375 380

Asn Arg Arg Leu Arg Gln Leu Leu Arg Trp Ala Arg Tyr His Ala Asn
385 390 395 400

Ala Phe Leu Leu Cys Ser Leu Ala Cys Ala Arg Phe Ala Ala Ser Arg
405 410 415

Thr Val Ile His Cys Ser Ile Tyr Pro Arg Phe Gly Pro Leu Ala Thr
 420 425 430

Val Thr Ala Ile Cys Leu Ile Leu His Thr Cys Thr Tyr Arg Arg Thr
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Glu Ala Asp Thr Thr Arg His Glu Asn Asp Asp Ala Arg Lys Val Met
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Glu Asp Met Ala Lys Arg Met Asp Asp Ser Ser Gly Ser Thr Leu
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Ser Thr Leu Thr Thr Asp Glu Thr Tyr His Thr Thr Glu Val Thr
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Ala Lys Lys Gly Ala Asn Leu Phe Lys
15 20

ccgctaaaa ttctcacggc gcatttatac ccgcagaact tttctgacca cttttag 155

acc cgc tgc gct cag tgc cac acc ctg aag gcc ggc gag ggc aac aag 203
Thr Arg Cys Ala Gln Cys His Thr Leu Lys Ala Gly Glu Gly Asn Lys
25 30 35

att ggc cct gag ctc cac ggt ctc ttc ggc cgc aag act ggt tcc gtc Ile Gly Pro Glu Leu His Gly Leu Phe Gly Arg Lys Thr Gly Ser Val 40 45 50	251
gct ggc tac tca tac acc gac gcc aac aag cag aag ggt atc gag tgg Ala Gly Tyr Ser Tyr Thr Asp Ala Asn Lys Gln Lys Gly Ile Glu Trp 55 60 65	299
aag gac gac act ctc gtacgtcacg ccaccgaaag attgaaatgt ccccgagacc Lys Asp Asp Thr Leu 70	354
ctccgctaac acgacacag ttc gag tac ctc gag aac ccc aag aag tac att Phe Glu Tyr Leu Glu Asn Pro Lys Lys Tyr Ile 75 80	406
ccc ggt acc aag atg gcc ttc ggt ggt ctc aag aag ccc aag gac cgc Pro Gly Thr Lys Met Ala Phe Gly Gly Leu Lys Lys Pro Lys Asp Arg 85 90 95 100	454
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Thr Gly Ser Val Ala Gly Tyr Ser Tyr Thr Asp Ala Asn Lys Gln Lys 50 55 60	
Gly Ile Glu Trp Lys Asp Asp Thr Leu Phe Glu Tyr Leu Glu Asn Pro 65 70 75 80	
Lys Lys Tyr Ile Pro Gly Thr Lys Met Ala Phe Gly Gly Leu Lys Lys 85 90 95	
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Leu Ile Arg Thr Pro Gln Thr Lys Gln Arg Leu Asn Phe His Ser Lys
20 25 30

acc cca aac cca gac gga tct aaa gat cca tct cca ccg gag cat cca 144
Thr Pro Asn Pro Asp Gly Ser Lys Asp Pro Ser Pro Pro Glu His Pro
35 40 45

gtt gaa gta atc ggc cgg atc cga gat tac cct gac cgg aaa gag aaa	192
Val Glu Val Ile Gly Arg Ile Arg Asp Tyr Pro Asp Arg Lys Glu Lys	
50 55 60	
tca cct tcg atc tta caa gtc aac aca gat aat caa acg gta cga gtc	240
Ser Pro Ser Ile Leu Gln Val Asn Thr Asp Asn Gln Thr Val Arg Val	
65 70 75 80	
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Arg Ala Asp Val Gly Tyr Arg Asp Phe Thr Leu Asp Gly Val Ser Phe	
85 90 95	
tcg gag caa gaa ggt ctt gaa gag ttc tac aag aag ttt ata gaa gag	336
Ser Glu Gln Glu Gly Leu Glu Phe Tyr Lys Lys Phe Ile Glu Glu	
100 105 110	
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Arg Ile Lys Gly Val Lys Val Gly Asn Lys Cys Thr Ile Met Met Tyr	
115 120 125	
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Gly Pro Thr Gly Ala Gly Lys Ser His Thr Met Phe Gly Cys Gly Lys	
130 135 140	
gag cct ggg att gtg tat cgt tct ttg aga gat ata ttg gga gat tct	480
Glu Pro Gly Ile Val Tyr Arg Ser Leu Arg Asp Ile Leu Gly Asp Ser	
145 150 155 160	
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Asp Gln Asp Gly Val Thr Phe Val Gln Val Thr Val Leu Glu Val Tyr	
165 170 175	
aat gag gag att tat gat ctt ctt tcg act aat agt aac aat tta	576
Asn Glu Glu Ile Tyr Asp Leu Leu Ser Thr Asn Ser Ser Asn Asn Leu	
180 185 190	
ggt att ggt tgg cct aaa gga gca agc act aag gtaaaagtttc ttgattgata	629
Gly Ile Gly Trp Pro Lys Gly Ala Ser Thr Lys	
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acttttagtat acattgaatt ggctttaaag gtgtgtactt tgttgttttg ttacag gtg	688
Val	
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Arg Leu Glu Val Met Gly Lys Lys Ala Lys Asn Ala Ser Phe Ile Ser	
205 210 215 220	
ggg aca gag gct ggg aag att tct aaa gaa att gtc aaa gtg gag aaa	784
Gly Thr Glu Ala Gly Lys Ile Ser Lys Glu Ile Val Lys Val Glu Lys	
225 230 235	
cgg aga att gtg aag agt aca ctt tgt aac gaa aga agt tct cgg agt	832
Arg Arg Ile Val Lys Ser Thr Leu Cys Asn Glu Arg Ser Ser Arg Ser	
240 245 250	
cac tgc att gtaagaacga tcttcttgat tgatgtgtat gcatagctt	881

His Cys Ile
 255

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Ile Ile
  
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 Leu Asp Val Pro Thr Val Gly Gly Arg Leu Met Leu Val Asp Met Ala
 260 265 270

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Gly Ser Glu Asn Ile Asp Gln Ala Gly Gln Thr Gly Phe Glu Ala Lys
  275 280 285
  
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atg caa gtaatgtttc ctctctcaat ttgtttgatt ctactaaagt tattgttagtt 1090
 Met Gln
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Thr Ala Lys Ile Asn
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cag gga aat att gca ctg aag cga gtt gtg gaa tct ata gca aat gga 1192
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 300 305 310

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gat tct cat gta ccc ttt aga gac agc aag ctg acc atg ctt ctc cag 1240
Asp Ser His Val Pro Phe Arg Asp Ser Lys Leu Thr Met Leu Leu Gln
  315 320 325
  
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gtgaaaattct tgccatcg tttatcttc tgaaaaatgt ttacgtgtt gcttggtttt 1300
  
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cttgaagata ttttgtttt tttctattct ctgaatgcag gac tct ttt gaa gat 1355
Asp Ser Phe Glu Asp
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gac aag tca aag att cta atg atc ctg tgt gcg agc ccg gat cca aag 1403
 Asp Lys Ser Lys Ile Leu Met Ile Leu Cys Ala Ser Pro Asp Pro Lys
 335 340 345

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gaa atg cac aag act ctc tgt act cta gag tat ggg gca aaa gca aag 1451
Glu Met His Lys Thr Leu Cys Thr Leu Glu Tyr Gly Ala Lys Ala Lys
  350 355 360 365
  
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tgc ata gtt cgt ggg tct cat act cca aac aaa gat aag tat ggg ggt 1499
Cys Ile Val Arg Gly Ser His Thr Pro Asn Lys Asp Lys Tyr Gly Gly
  370 375 380
  
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gat gag tct gct tct gct gtg att ttg gga tca aga ata gct gcc atg 1547
Asp Glu Ser Ala Ser Ala Val Ile Leu Gly Ser Arg Ile Ala Ala Met
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gat gag ttc att atc aaa ctc cag tct gag aag aag caa aaa gaa aaa 1595
Asp Glu Phe Ile Ile Lys Leu Gln Ser Glu Lys Lys Gln Lys Glu Lys
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79

Glu Arg Asn Glu Ala Gln Lys Gln Leu Lys Lys Lys Glu Glu Glu Val		
415	420	425
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Ala Ala Leu Arg Ser Leu Leu Thr Gln Arg Glu Ala Cys Ala Thr Asn		
430	435	440
445		
gaa gag gag ata aaa gag aaa gta aac gag aga acc cag ctt ttg aag 1739		
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1787		
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465	470	475
1835		
ttt gtt gag atg gag aga agg aga atg gag gaa agg ata gtt cag cag		
Phe Val Glu Met Glu Arg Arg Met Glu Glu Arg Ile Val Gln Gln		
480	485	490
1883		
caa gag gaa ctg gag atg atg agg aga cgg tta gag gaa atc gag gtt		
Gln Glu Glu Leu Glu Met Met Arg Arg Arg Leu Glu Glu Ile Glu Val		
495	500	505
1931		
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Glu Phe Arg Arg Ser Asn Gly Gly Ser Val Asp Glu Thr Ser Gly Phe		
510	515	520
525		
1979		
gcc aaa aga ctc agg agt ctt tac tct gat gat gat cct ggt atg gtg		
Ala Lys Arg Leu Arg Ser Leu Tyr Ser Asp Asp Asp Pro Gly Met Val		
530	535	540
2027		
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Lys Ser Met Asp Leu Asp Met Gly Asp Pro Glu Pro Val Lys Gln Val		
545	550	555
2075		
tgg gga gct gtt tca cac caa tca agc aac act att agt agc aac ttc		
Trp Gly Ala Val Ser His Gln Ser Ser Asn Thr Ile Ser Ser Asn Phe		
560	565	570
2123		
act aac ctt ttg caa ccg aag cct tca gag aat atg ctt aca cag atg		
Thr Asn Leu Leu Gln Pro Lys Pro Ser Glu Asn Met Leu Thr Gln Met		
575	580	585
2171		
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Tyr Pro Asp Arg Val Cys Leu Ser Thr Val Phe Glu Glu Glu Val		
590	595	600
605		
2219		
gaa gaa gag gaa aaa gtg ata gtc gag gat aaa agc atc tgc ttg		
Glu Glu Glu Glu Lys Val Ile Val Glu Asp Lys Ser Ile Cys Leu		
610	615	620
2267		
ata aca aca cca atg cct agt ttg aac tct gaa ggt ttg ggt aaa gag		
Ile Thr Thr Pro Met Pro Ser Leu Asn Ser Glu Gly Leu Gly Lys Glu		
625	630	635
2315		
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655	660	665	
tct caa cac agt gga cag gag gag gat caa gcc aat att gca tca cct Ser Gln His Ser Gly Gln Glu Glu Asp Gln Ala Asn Ile Ala Ser Pro			2411
670	675	680	685
gat aag aaa gac aat cag ttc ttt tct att acg aat aag gcc gaa gca Asp Lys Lys Asp Asn Gln Phe Phe Ser Ile Thr Asn Lys Ala Glu Ala			2459
690	695	700	
cta gca gta gaa gaa gca aag gaa aac aat atc tca gtc gat caa agg Leu Ala Val Glu Glu Ala Lys Glu Asn Asn Ile Ser Val Asp Gln Arg			2507
705	710	715	
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720	725	730	
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735	740	745	
cta gct gac ttg agg aag ctt att gag atc tac ctt gga tct gat aat Leu Ala Asp Leu Arg Lys Leu Ile Glu Ile Tyr Leu Gly Ser Asp Asn			2651
750	755	760	765
cag gct ttt acc ttt ctc aag ctc ggg gta ata aac ttg aac caa caa Gln Ala Phe Thr Phe Leu Lys Leu Gly Val Ile Asn Leu Asn Gln Gln			2699
770	775	780	
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850	855	860	

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Ile Leu Leu Lys Thr Glu
865

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 870 875 880

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His Phe Leu Ile Leu Phe Pro Ar
885 890

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895 900 905

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 His Gln Thr Ser Pro Ser Leu Ser Ser Phe Pro Leu Leu Ser Arg Ala
 910 915 920

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925

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930 935

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tac gca gcc act tgt ctc tcc gtc gaa gac gcc gtc aac gct cga tca	100
Tyr Ala Ala Thr Cys Leu Ser Val Glu Asp Ala Val Asn Ala Arg Ser	
10 15 20 25	

ata agc aat tgc aat gtc ctc gca ttc tcc ggc atc aaa aca tcc ccg	148
Ile Ser Asn Cys Asn Val Leu Ala Phe Ser Gly Ile Lys Thr Ser Pro	
30 35 40	

gaa acc gcc ttg gaa atc ttc gac gct tgg atc aaa act cct ttc aaa	196
Glu Thr Ala Leu Glu Ile Phe Asp Ala Trp Ile Lys Thr Pro Phe Lys	
45 50 55	

tct cct tgt cct gcg tcc gga tcc gaa cca tgg agc tca gtt atc tct	244
Ser Pro Cys Pro Ala Ser Gly Ser Glu Pro Trp Ser Ser Val Ile Ser	
60 65 70	

tcc ttc ctc gac aat tct ctc tcc gag atg tct cag att gga aag tca	292
Ser Phe Leu Asp Asn Ser Leu Ser Glu Met Ser Gln Ile Gly Lys Ser	
75 80 85	

acc gcc ggc gat tca aca acc aag aag atc gat gaa aca acc gcg tct	340
Thr Ala Gly Asp Ser Thr Thr Lys Lys Ile Asp Glu Thr Thr Ala Ser	
90 95 100 105	

tgc gta att tgc tgc ttg gcg aag aac aga gag ttc act cca gtg gac 388

Cys Val Ile Cys Cys Leu Ala Lys Asn Arg Glu Phe Thr Pro Val Asp			
110	115	120	
atc atg ccg gga ggc tcg atg aag atc gtt aga gag acg ccg acg tcg			436
Ile Met Pro Gly Gly Ser Met Lys Ile Val Arg Glu Thr Pro Thr Ser			
125	130	135	
gcg att gta aga ttc aaa gcg gga agt gtg gaa ccg gcg cat cac cac			484
Ala Ile Val Arg Phe Lys Ala Gly Ser Val Glu Pro Ala His His His			
140	145	150	
aca ttc ggc cat gac ctt gta gtc ata aag gga aag aaa agt gtg tgg			532
Thr Phe Gly His Asp Leu Val Val Ile Lys Gly Lys Ser Val Trp			
155	160	165	
aat ctg agc aag aag gag aga gct gat ctc gtt gac ggc gat tac cta			580
Asn Leu Ser Lys Lys Glu Arg Ala Asp Leu Val Asp Gly Asp Tyr Leu			
170	175	180	185
tcc act ccc gcc ggt gat gtt cac cga gtc aaa tat cac gaa gac act			628
Phe Thr Pro Ala Gly Asp Val His Arg Val Lys Tyr His Glu Asp Thr			
190	195	200	
gag ttc ttc atc act tgg gat ggc cat tgg gac ata ttc ctt gac gaa			676
Glu Phe Phe Ile Thr Trp Asp Gly His Trp Asp Ile Phe Leu Asp Glu			
205	210	215	
gac ctc gaa act gca aag aaa gcc atc gaa gaa gaa gct tga			718
Asp Leu Glu Thr Ala Lys Lys Ala Ile Glu Glu Glu Ala			
220	225	230	
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Ala Phe Ser Gly Ile Lys Thr Ser Pro Glu Thr Ala Leu Glu Ile Phe			
35	40	45	
Asp Ala Trp Ile Lys Thr Pro Phe Lys Ser Pro Cys Pro Ala Ser Gly			
50	55	60	
Ser Glu Pro Trp Ser Ser Val Ile Ser Ser Phe Leu Asp Asn Ser Leu			
65	70	75	80
Ser Glu Met Ser Gln Ile Gly Lys Ser Thr Ala Gly Asp Ser Thr Thr			
85	90	95	

Lys Lys Ile Asp Glu Thr Thr Ala Ser Cys Val Ile Cys Cys Leu Ala
 100 105 110
 Lys Asn Arg Glu Phe Thr Pro Val Asp Ile Met Pro Gly Gly Ser Met
 115 120 125
 Lys Ile Val Arg Glu Thr Pro Thr Ser Ala Ile Val Arg Phe Lys Ala
 130 135 140
 Gly Ser Val Glu Pro Ala His His His Thr Phe Gly His Asp Leu Val
 145 150 155 160
 Val Ile Lys Gly Lys Ser Val Trp Asn Leu Ser Lys Lys Glu Arg
 165 170 175
 Ala Asp Leu Val Asp Gly Asp Tyr Leu Phe Thr Pro Ala Gly Asp Val
 180 185 190
 His Arg Val Lys Tyr His Glu Asp Thr Glu Phe Phe Ile Thr Trp Asp
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 Gly His Trp Asp Ile Phe Leu Asp Glu Asp Leu Glu Thr Ala Lys Lys
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 Ala Ile Glu Glu Glu Ala
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 Pro Ile Ser Ser Thr Leu Asn Gln His Leu Val Asp Tyr Pro Thr Pro
 15 20 25
 agc aat ctt agt tat tgg tgg ggg ttc ggt ccg tta gct ggt att tgt 146
 Ser Asn Leu Ser Tyr Trp Trp Gly Phe Gly Pro Leu Ala Gly Ile Cys
 30 35 40 45
 tta gtc att cag ata gtg act ggc gtt ttt tta gct atg cat tac aca 194
 Leu Val Ile Gln Ile Val Thr Gly Val Phe Leu Ala Met His Tyr Thr
 50 55 60
 cct cat gtg gat tta gct ttc aac agc gta gaa cac att atg aga gat 242

Pro His Val Asp Leu Ala Phe Asn Ser Val Glu His Ile Met Arg Asp			
65	70	75	
gtt gaa ggg ggc tgg ttg ctc cgt tat atg cat gct aat ggg gca agt		290	
Val Glu Gly Gly Trp Leu Leu Arg Tyr Met His Ala Asn Gly Ala Ser			
80	85	90	
atg ttt ctt att gtg gtt tac ctt cat att ttt cgt ggt cta tat cat		338	
Met Phe Leu Ile Val Val Tyr Leu His Ile Phe Arg Gly Leu Tyr His			
95	100	105	
gcg agt tat agc agt cct agg gaa ttt gtt tgg tgt ctt gga gtt gta		386	
Ala Ser Tyr Ser Ser Pro Arg Glu Phe Val Trp Cys Leu Gly Val Val			
110	115	120	125
atc ttc cta tta atg att gtg aca gct ttt ata gga tat gta cta cct		434	
Ile Phe Leu Leu Met Ile Val Thr Ala Phe Ile Gly Tyr Val Leu Pro			
130	135	140	
tgg ggt cag atg agc ttt tgg gga gct aca gta att aca agc tta gct		482	
Trp Gly Gln Met Ser Phe Trp Gly Ala Thr Val Ile Thr Ser Leu Ala			
145	150	155	
agc gcc ata cct gta gta gga gat acc ata gtg act tgg ctt tgg ggt		530	
Ser Ala Ile Pro Val Val Gly Asp Thr Ile Val Thr Trp Leu Trp Gly			
160	165	170	
ggt ttc tcc gtg gac aat gcc acc tta aat cgt ttt ttt agt ctt cat		578	
Gly Phe Ser Val Asp Asn Ala Thr Leu Asn Arg Phe Phe Ser Leu His			
175	180	185	
cat tta ctc ccc ttt att tta gta ggc gcc agt ctt ctt cat ctg gcc		626	
His Leu Leu Pro Phe Ile Leu Val Gly Ala Ser Leu Leu His Leu Ala			
190	195	200	205
gca ttg cat caa tat gga tca aat aat cca ttg ggt gta cat tct gag		674	
Ala Leu His Gln Tyr Gly Ser Asn Asn Pro Leu Gly Val His Ser Glu			
210	215	220	
atg gat aaa ata gct ttt tac cct tat ttt tat gtc aag gat cta gtt		722	
Met Asp Lys Ile Ala Phe Tyr Pro Tyr Phe Tyr Val Lys Asp Leu Val			
225	230	235	
ggt tgg gta gct ttt gct atc ttt tct att tgg att ttt tat gct		770	
Gly Trp Val Ala Phe Ala Ile Phe Phe Ser Ile Trp Ile Phe Tyr Ala			
240	245	250	
cct aat gtt ttg gga cat ccc gac aat tat ata cct gct aat ccg atg		818	
Pro Asn Val Leu Gly His Pro Asp Asn Tyr Ile Pro Ala Asn Pro Met			
255	260	265	
tcc acc ccg cct cat att gtg ccg gaa tgg tat ttc cta ccg atc cat		866	
Ser Thr Pro Pro His Ile Val Pro Glu Trp Tyr Phe Leu Pro Ile His			
270	275	280	285
gcc att ctt cgt agt ata cct gac aaa gcg gga ggt gta gcc gca ata		914	
Ala Ile Leu Arg Ser Ile Pro Asp Lys Ala Gly Gly Val Ala Ala Ile			

290	295	300	
gca cca gtt ttt ata tgt ctc ttg gct tta cct ttt aaa	agt atg		962
Ala Pro Val Phe Ile Cys Leu Leu Ala Leu Pro Phe Phe Lys Ser Met			
305	310	315	
tat gtg cgt agt tca agt ttt cga ccg att cac caa gga atg ttt tgg			1010
Tyr Val Arg Ser Ser Ser Phe Arg Pro Ile His Gln Gly Met Phe Trp			
320	325	330	
ttg ctt ttg gcg gat tgc tta cta cta ggt tgg atc gga tgg caa cct			1058
Leu Leu Leu Ala Asp Cys Leu Leu Leu Gly Trp Ile Gly Cys Gln Pro			
335	340	345	
gtg gag gct cca ttt gtt act att gga caa att tct cct ttg gtt ttc			1106
Val Glu Ala Pro Phe Val Thr Ile Gly Gln Ile Ser Pro Leu Val Phe			
350	355	360	365
ttc ttg ttc ttt gcc ata acg ccc att ctg gga cga gtt gga aga gga			1154
Phe Leu Phe Phe Ala Ile Thr Pro Ile Leu Gly Arg Val Gly Arg Gly			
370	375	380	
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Ile Pro Asn Ser Tyr Thr Asp Glu Thr Asp His Thr			
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20	25	30	
Ser Tyr Trp Trp Gly Phe Gly Pro Leu Ala Gly Ile Cys Leu Val Ile			
35	40	45	
Gln Ile Val Thr Gly Val Phe Leu Ala Met His Tyr Thr Pro His Val			
50	55	60	
Asp Leu Ala Phe Asn Ser Val Glu His Ile Met Arg Asp Val Glu Gly			
65	70	75	80
Gly Trp Leu Leu Arg Tyr Met His Ala Asn Gly Ala Ser Met Phe Leu			
85	90	95	
Ile Val Val Tyr Leu His Ile Phe Arg Gly Leu Tyr His Ala Ser Tyr			
100	105	110	
Ser Ser Pro Arg Glu Phe Val Trp Cys Leu Gly Val Val Ile Phe Leu			
115	120	125	

Leu Met Ile Val Thr Ala Phe Ile Gly Tyr Val Leu Pro Trp Gly Gln
 130 135 140
 Met Ser Phe Trp Gly Ala Thr Val Ile Thr Ser Leu Ala Ser Ala Ile
 145 150 155 160
 Pro Val Val Gly Asp Thr Ile Val Thr Trp Leu Trp Gly Gly Phe Ser
 165 170 175
 Val Asp Asn Ala Thr Leu Asn Arg Phe Phe Ser Leu His His Leu Leu
 180 185 190
 Pro Phe Ile Leu Val Gly Ala Ser Leu Leu His Leu Ala Ala Leu His
 195 200 205
 Gln Tyr Gly Ser Asn Asn Pro Leu Gly Val His Ser Glu Met Asp Lys
 210 215 220
 Ile Ala Phe Tyr Pro Tyr Phe Tyr Val Lys Asp Leu Val Gly Trp Val
 225 230 235 240
 Ala Phe Ala Ile Phe Phe Ser Ile Trp Ile Phe Tyr Ala Pro Asn Val
 245 250 255
 Leu Gly His Pro Asp Asn Tyr Ile Pro Ala Asn Pro Met Ser Thr Pro
 260 265 270
 Pro His Ile Val Pro Glu Trp Tyr Phe Leu Pro Ile His Ala Ile Leu
 275 280 285
 Arg Ser Ile Pro Asp Lys Ala Gly Gly Val Ala Ala Ile Ala Pro Val
 290 295 300
 Phe Ile Cys Leu Leu Ala Leu Pro Phe Phe Lys Ser Met Tyr Val Arg
 305 310 315 320
 Ser Ser Ser Phe Arg Pro Ile His Gln Gly Met Phe Trp Leu Leu Leu
 325 330 335
 Ala Asp Cys Leu Leu Leu Gly Trp Ile Gly Cys Gln Pro Val Glu Ala
 340 345 350
 Pro Phe Val Thr Ile Gly Gln Ile Ser Pro Leu Val Phe Phe Leu Phe
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 370 375 380
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 385 390

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1			5					10					15				
cga	gga	aat	tac	gca	gct	aca	ctc	gat	gtg	tcg	tat	ccg	gta	ttc	ccg		96
Arg	Gly	Asn	Tyr	Ala	Ala	Thr	Leu	Asp	Val	Ser	Tyr	Pro	Val	Phe	Pro		
			20					25					30				
caa	aat	aaa	gat	ggc	cgt	gca	ctt	cag	aaa	gtt	ctc	gga	acc	att	cgt		144
Gln	Asn	Lys	Asp	Gly	Arg	Ala	Leu	Gln	Lys	Val	Leu	Gly	Thr	Ile	Arg		
			35					40					45				
aac	gga	gat	ttg	gct	gtt	tcg	gct	cct	aaa	aca	agt	ctt	agg	gca	ggt		192
Asn	Gly	Asp	Leu	Ala	Val	Ser	Ala	Pro	Lys	Thr	Ser	Leu	Arg	Ala	Gly		
			50				55					60					
att	ttc	ggt	gaa	ggt	tcc	agc	ttg	gtc	gat	cag	atg	ccc	tgt	aaa	gtt		240
Ile	Phe	Gly	Glu	Gly	Ser	Ser	Leu	Val	Asp	Gln	Met	Pro	Cys	Lys	Val		
			65				70				75			80			
tac	gtg	gcf	ttc	cac	aaa	gaa	tca	tac	tcg	tcg	ctt	acc	ggg	cta	agc		288
Tyr	Val	Ala	Phe	His	Lys	Glu	Ser	Tyr	Cys	Ser	Leu	Thr	Gly	Leu	Ser		
			85					90					95				
aaa	cgc	gga	gtc	gca	ata	aac	gaa	gca	agt	ctt	tcc	ctg	gtc	gga	atc		336
Lys	Arg	Gly	Val	Ala	Ile	Asn	Glu	Ala	Ser	Leu	Ser	Leu	Val	Gly	Ile		
			100					105					110				
act	aaa	gtt	aga	gcc	ccc	gtc	gga	aat	acc	gtt	gga	gcf	gaa	gca	acc		384
Thr	Lys	Val	Arg	Ala	Pro	Val	Gly	Asn	Thr	Val	Gly	Ala	Glu	Ala	Thr		
			115				120					125					
gta	tac	ata	ggt	agt	cca	aaa	cct	tat	aca	gag	tgt	agt	act	cca	aat		432
Val	Tyr	Ile	Gly	Ser	Pro	Lys	Pro	Tyr	Thr	Glu	Cys	Ser	Thr	Pro	Asn		
			130				135				140						
aaa	atg	tat	gcf	gtt	gca	gct	ggt	ttc	aag	gtg	gca	agt	ttc	gcc	gct		480
Lys	Met	Tyr	Ala	Val	Ala	Ala	Gly	Phe	Lys	Val	Ala	Ser	Phe	Ala	Ala		
			145					150				155		160			
agt	acg	tgc	gta	cgt	ccg	cct	gca	cgt	gca	cgt	cgt	acg	ctg	acc	gtg		528
Ser	Thr	Cys	Val	Arg	Pro	Pro	Ala	Arg	Ala	Arg	Arg	Thr	Leu	Thr	Val		
			165					170					175				
acg	tcg	acc	gtg	acg	ctg	tct	atg	gca	act	ggt	aaa	tgc	gta	aat	aca		576
Thr	Ser	Thr	Val	Thr	Leu	Ser	Met	Ala	Thr	Gly	Lys	Cys	Val	Asn	Thr		
			180					185					190				
gga	aac	gaa	cca	gta	tct	aaa	cct	aca	gga	gta	cgt	atg	atg	tta	att		624
Gly	Asn	Glu	Pro	Val	Ser	Lys	Pro	Thr	Gly	Val	Arg	Met	Met	Leu	Ile		
			195					200					205				

cct ctc gat gct act ctc att aaa gta tgg act ggg gaa gta aaa aaa Pro Leu Asp Ala Thr Leu Ile Lys Val Trp Thr Gly Glu Val Lys Lys 210 215 220	672
gcg ata gtt tcc cgg cct gca aaa att ttc aat agc gta gga aat tta Ala Ile Val Ser Arg Pro Ala Lys Ile Phe Asn Ser Val Gly Asn Leu 225 230 235 240	720
gaa cgt cct tca att tcg cat tct tgt gga caa ggt ttg gat gaa gct Glu Arg Pro Ser Ile Ser His Ser Cys Gly Gln Gly Leu Asp Glu Ala 245 250 255	768
gcc gct tat atc aag ggt aga ctt tct cca atc gtt aaa gca gaa aga Ala Ala Tyr Ile Lys Gly Arg Leu Ser Pro Ile Val Lys Ala Glu Arg 260 265 270	816
att aaa gtt ttg gtt aaa gac gag cac gaa gta aaa gaa ctt ctt Ile Lys Val Leu Val Lys Asp Glu His Glu Val Lys Glu Leu Leu 275 280 285	864
caa gaa ggt tac gaa gaa atc gtc ggt gag tct cca agt ttc aat tta Gln Glu Gly Tyr Glu Glu Ile Val Gly Glu Ser Pro Ser Phe Asn Leu 290 295 300	912
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ccg tgc agt gcg gca aaa gca aac ctt gca acc tac tat ttt tca aca Pro Cys Ser Ala Ala Lys Ala Asn Leu Ala Thr Tyr Tyr Phe Ser Thr 325 330 335	1008
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aaa gat act gat aag agc tat ctg cga gaa cgt aga aaa aga gta gag Lys Asp Thr Asp Lys Ser Tyr Leu Arg Glu Arg Arg Lys Arg Val Glu 355 360 365	1104
gct act acg ttg cgt gca ccg ttc gtg gtc cag ctg acc gtg cgt agt Ala Thr Thr Leu Arg Ala Pro Phe Val Val Gln Leu Thr Val Arg Ser 370 375 380	1152
cgt acg acg atg atc gcc gtt ggt gaa agc aac gca aac tga Arg Thr Thr Met Ile Ala Val Gly Glu Ser Asn Ala Asn 385 390 395	1194
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Gln	Asn	Lys	Asp Gly Arg Ala Leu Gln Lys Val Leu Gly Thr Ile Arg		
		35	40	45	
Asn	Gly	Asp	Leu Ala Val Ser Ala Pro Lys Thr Ser Leu Arg Ala Gly		
		50	55	60	
Ile	Phe	Gly	Glu Gly Ser Ser Leu Val Asp Gln Met Pro Cys Lys Val		
		65	70	75	80
Tyr	Val	Ala	Phe His Lys Glu Ser Tyr Cys Ser Leu Thr Gly Leu Ser		
		85	90	95	
Lys	Arg	Gly	Val Ala Ile Asn Glu Ala Ser Leu Ser Leu Val Gly Ile		
		100	105	110	
Thr	Lys	Val	Arg Ala Pro Val Gly Asn Thr Val Gly Ala Glu Ala Thr		
		115	120	125	
Val	Tyr	Ile	Gly Ser Pro Lys Pro Tyr Thr Glu Cys Ser Thr Pro Asn		
		130	135	140	
Lys	Met	Tyr	Ala Val Ala Ala Gly Phe Lys Val Ala Ser Phe Ala Ala		
		145	150	155	160
Ser	Thr	Cys	Val Arg Pro Pro Ala Arg Ala Arg Arg Thr Leu Thr Val		
		165	170	175	
Thr	Ser	Thr	Val Thr Leu Ser Met Ala Thr Gly Lys Cys Val Asn Thr		
		180	185	190	
Gly	Asn	Glu	Pro Val Ser Lys Pro Thr Gly Val Arg Met Met Leu Ile		
		195	200	205	
Pro	Leu	Asp	Ala Thr Leu Ile Lys Val Trp Thr Gly Glu Val Lys Lys		
		210	215	220	
Ala	Ile	Val	Ser Arg Pro Ala Lys Ile Phe Asn Ser Val Gly Asn Leu		
		225	230	235	240
Glu	Arg	Pro	Ser Ile Ser His Ser Cys Gly Gln Gly Leu Asp Glu Ala		
		245	250	255	
Ala	Ala	Tyr	Ile Lys Gly Arg Leu Ser Pro Ile Val Lys Ala Glu Arg		
		260	265	270	
Ile	Lys	Val	Leu Val Lys Asp Glu His Glu Glu Val Lys Glu Leu Leu		
		275	280	285	
Gln	Glu	Gly	Tyr Glu Glu Ile Val Gly Glu Ser Pro Ser Phe Asn Leu		
		290	295	300	
Ala	Gln	Glu	Ala Trp Glu Lys Ala Glu Arg Arg Ala Lys Gly Gln Ser		

305	310	315	320
Pro Cys Ser Ala Ala Lys Ala Asn Leu Ala Thr Tyr Tyr Phe Ser Thr			
325	330	335	
Gly Asp Phe Glu Lys Ser Ile Lys Leu Tyr Glu Glu Pro Met Gly Leu			
340	345	350	
Lys Asp Thr Asp Lys Ser Tyr Leu Arg Glu Arg Arg Lys Arg Val Glu			
355	360	365	
Ala Thr Thr Leu Arg Ala Pro Phe Val Val Gln Leu Thr Val Arg Ser			
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gtc gtc ttt tcc gtc gcg ctt ctt ctg ttc tac ttc tct gaa act tct	97		
Val Val Phe Ser Val Ala Leu Leu Leu Phe Tyr Phe Ser Glu Thr Ser			
20	25	30	
cta gga gct cct tgt ccc atc aat ggc ttg cca atc gtg agg aat att	145		
Leu Gly Ala Pro Cys Pro Ile Asn Gly Leu Pro Ile Val Arg Asn Ile			
35	40	45	
agt gac ctt cct cag gat aac tat gga aga cca ggt ctt tcc cac atg	193		
Ser Asp Leu Pro Gln Asp Asn Tyr Gly Arg Pro Gly Leu Ser His Met			
50	55	60	
act gtt gct ggc tcc gta ttg cat gga atg aaa gag gtt gaa ata tgg	241		
Thr Val Ala Gly Ser Val Leu His Gly Met Lys Glu Val Glu Ile Trp			
65	70	75	
ctt cag aca ttt gct cca ggt tca gag aca cca att cac agg cac tcc	289		
Leu Gln Thr Phe Ala Pro Gly Ser Glu Thr Pro Ile His Arg His Ser			
80	85	90	95
tgt gaa gag gtt ttt gtt gtc cta aag ggc agt ggt act ctg tat ctc	337		
Cys Glu Glu Val Phe Val Val Leu Lys Gly Ser Gly Thr Leu Tyr Leu			
100	105	110	

gct gaa aca cat gga aat ttc cct ggg aaa cca atc gaa ttt cca atc 385
 Ala Glu Thr His Gly Asn Phe Pro Gly Lys Pro Ile Glu Phe Pro Ile
 115 120 125

 ttt gcc aac agt aca att cat att ccg atc aat gat gct cat cag gtc 433
 Phe Ala Asn Ser Thr Ile His Ile Pro Ile Asn Asp Ala His Gln Val
 130 135 140

 aaa aac acc ggt cat gag gac ctg cag gtg ttg gtt atc ata tct cgg 481
 Lys Asn Thr Gly His Glu Asp Leu Gln Val Leu Val Ile Ile Ser Arg
 145 150 155

 ccg cct att aaa atc ttc atc tac gaa gac tgg ttt atg cca cac act 529
 Pro Pro Ile Lys Ile Phe Ile Tyr Glu Asp Trp Phe Met Pro His Thr
 160 165 170 175

 gct gca agg ctg aag ttc cct tac tat tgg gat gag caa tgc att caa 577
 Ala Ala Arg Leu Lys Phe Pro Tyr Tyr Trp Asp Glu Gln Cys Ile Gln
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 gaa tca caa aaa gac gag ctt taa agcaaagtcc 611
 Glu Ser Gln Lys Asp Glu Leu
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 35 40 45

 Asp Leu Pro Gln Asp Asn Tyr Gly Arg Pro Gly Leu Ser His Met Thr
 50 55 60

 Val Ala Gly Ser Val Leu His Gly Met Lys Glu Val Glu Ile Trp Leu
 65 70 75 80

 Gln Thr Phe Ala Pro Gly Ser Glu Thr Pro Ile His Arg His Ser Cys
 85 90 95

 Glu Glu Val Phe Val Val Leu Lys Gly Ser Gly Thr Leu Tyr Leu Ala
 100 105 110

 Glu Thr His Gly Asn Phe Pro Gly Lys Pro Ile Glu Phe Pro Ile Phe
 115 120 125

 Ala Asn Ser Thr Ile His Ile Pro Ile Asn Asp Ala His Gln Val Lys
 130 135 140

Asn Thr Gly His Glu Asp Leu Gln Val Leu Val Ile Ile Ser Arg Pro
 145 150 155 160
 Pro Ile Lys Ile Phe Ile Tyr Glu Asp Trp Phe Met Pro His Thr Ala
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 180 185 190
 Ser Gln Lys Asp Glu Leu
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Met	Pro	Arg	Arg	Arg	Thr	Cys	Cys	Arg	Arg	Glu	Phe	Gly	Pro	Thr	Gln	
1	5	10	15													

cca tgt aga ggc gcg tca atc act gga tct cta cgt gac cgt cga ccg 96
 Pro Cys Arg Gly Ala Ser Ile Thr Gly Ser Leu Arg Asp Arg Arg Pro
 20 25 30

acc gct atc ctt atc gga acc ctc acc gct tta ggc ggt gga gtt aga 144
 Thr Ala Ile Leu Ile Gly Thr Leu Thr Ala Leu Gly Gly Val Arg
 35 40 45

tgt ggc tct tgc ccc agt gtc gac cgt tgc gga cac gca agt gcc gcc 192
 Cys Gly Ser Cys Pro Ser Val Asp Arg Cys Gly His Ala Ser Ala Ala
 50 55 60

ata gcg cgt gat agc tgt gcc gtg ttc gca tgg aag cga ggt acg cga 240
 Ile Ala Arg Asp Ser Cys Ala Val Phe Ala Trp Lys Arg Gly Thr Arg
 65 70 75 80

caa gag tac tgg tgc tcg act gaa ccg acc ctt gac tgg ggc ccc ggt 288
 Gln Glu Tyr Trp Cys Ser Thr Glu Pro Thr Leu Asp Trp Gly Pro Gly
 85 90 95

ggt gga ccc gac ttc gat tgt gat gat ggt gac gat ccg ctt ttg 336
 Gly Gly Pro Asp Phe Asp Cys Asp Asp Gly Gly Asp Asp Pro Leu Leu
 100 105 110

att caa gat ggc gta aaa gct gcg gag gaa tat gct aaa tct gga aaa 384
 Ile Gln Asp Gly Val Lys Ala Ala Glu Glu Tyr Ala Lys Ser Gly Lys
 115 120 125

gtt cca gat cca agc tgt act gat aat gct gag ttt caa gtt gtg ctt	432
Val Pro Asp Pro Ser Cys Thr Asp Asn Ala Glu Phe Gln Val Val Leu	
130 135 140	
att att att agg gag ggg ttg aaa act gat cct tta aaa tac act aag	480
Ile Ile Ile Arg Glu Gly Leu Lys Thr Asp Pro Leu Lys Tyr Thr Lys	
145 150 155 160	
cga ccc agt tgc ctt ggt gtt tct gag gaa act act act ggt gtt	528
Arg Pro Ser Cys Leu Val Gly Val Ser Glu Glu Thr Thr Gly Val	
165 170 175	
aag aga agt taccaa atg cag ccg aaa tgt act ttg ctt ttg cat gct	576
Lys Arg Ser Tyr Gln Met Gln Pro Lys Cys Thr Leu Leu Leu His Ala	
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act gat gtt tgt gac acc gtc atc aag agc aag att gat aac ttg tac	624
Thr Asp Val Cys Asp Thr Val Ile Lys Ser Lys Ile Asp Asn Leu Tyr	
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Gly Cys Arg His Ser Leu Ser Asp Gly Leu Met Arg Ala Thr Asp Val	
210 215 220	
cgt cgc ccc tgc aag gta gcg ctt gta ggc ggt tac gga gat gtc ttt	720
Arg Arg Pro Cys Lys Val Ala Leu Val Gly Gly Tyr Gly Asp Val Phe	
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Lys Gly Trp Val Ala Ala Leu Lys Gln Ala Gly Ala Arg Val Ile Val	
245 250 255	
act gag atc ccg caa atc tgt gcc gtc caa gct acc atg gaa ggt agt	816
Thr Glu Ile Pro Gln Ile Cys Ala Val Gln Ala Thr Met Glu Gly Ser	
260 265 270	
tcg gtc ctt acc ctt gag gat gtc gtt tca gat gtt gat cgc ttc gtt	864
Ser Val Leu Thr Leu Glu Asp Val Val Ser Asp Val Asp Arg Phe Val	
275 280 285	
acg aca acc ggt aac aag gac ctc atc atg gtt gac cac atg agg cga	912
Thr Thr Gly Asn Lys Asp Leu Ile Met Val Asp His Met Arg Arg	
290 295 300	
atg aag aac cag gcc ata gtt tgc aac att cga cgt ttc gac aat gaa	960
Met Lys Asn Gln Ala Ile Val Cys Asn Ile Arg Arg Phe Asp Asn Glu	
305 310 315 320	
atc gac atg cgc agt ctc gag acc ttc cct gga gtg aag cggt atc aca	1008
Ile Asp Met Arg Ser Leu Glu Thr Phe Pro Gly Val Lys Arg Ile Thr	
325 330 335	
atc aag gcc cag act gac aga tgg gtc ttt cgc gac acc aac aga ggt	1056
Ile Lys Ala Gln Thr Asp Arg Trp Val Phe Arg Asp Thr Asn Arg Gly	
340 345 350	
atc att gtc cca gcc gag ggg cgt ctc atg acg atg gga tgc gcc act	1104

Ile Ile Val Pro Ala Glu Gly Arg Leu Met Thr Met Gly Cys Ala Thr		
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Gly His Pro Ser Phe Arg Thr Ser Cys Ser Phe Thr Asn Gln Val Ser		
370	375	380
tct cag ctc gag ttg tgg cgg gag aag agc acc ggc aag tat gag aag		1200
Ser Gln Leu Glu Leu Trp Arg Glu Lys Ser Thr Gly Lys Tyr Glu Lys		
385	390	395
Lys Val Tyr Val Phe Pro Lys His Leu Glu Lys Lys Val Ala Ala Leu		
405	410	415
aaa gtg tac gtc ttc cca aag cac ctt gag aag aag gtt gcc gcc ctt		1248
Lys Val Tyr Val Phe Pro Lys His Leu Glu Lys Lys Val Ala Ala Leu		
420	425	430
cat ctc gta aag ctc gga gca agg ctc act aag ctt agt cgg tgc acg		1296
His Leu Val Lys Leu Gly Ala Arg Leu Thr Lys Leu Ser Arg Cys Thr		
420	425	430
ttg ttg tgc acg gac gac cca gtt gaa ggt cgt aaa gag cct cct cac		1344
Leu Leu Cys Thr Asp Asp Pro Val Glu Gly Arg Lys Glu Pro Pro His		
435	440	445
cgt gct ggc agc cct gaa ccg tgc cag ctg cag ctg acc gtg ttc agg		1392
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Thr Ala Ile Leu Ile Gly Thr Leu Thr Ala Leu Gly Gly Val Arg		
35	40	45
Cys Gly Ser Cys Pro Ser Val Asp Arg Cys Gly His Ala Ser Ala Ala		
50	55	60
Ile Ala Arg Asp Ser Cys Ala Val Phe Ala Trp Lys Arg Gly Thr Arg		
65	70	75
		80
Gln Glu Tyr Trp Cys Ser Thr Glu Pro Thr Leu Asp Trp Gly Pro Gly		
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Gly Gly Pro Asp Phe Asp Cys Asp Gly Gly Asp Asp Pro Leu Leu		

100	105	110
Ile Gln Asp Gly Val Lys Ala Ala Glu Glu Tyr Ala Lys Ser Gly Lys		
115	120	125
Val Pro Asp Pro Ser Cys Thr Asp Asn Ala Glu Phe Gln Val Val Leu		
130	135	140
Ile Ile Ile Arg Glu Gly Leu Lys Thr Asp Pro Leu Lys Tyr Thr Lys		
145	150	155
Arg Pro Ser Cys Leu Val Gly Val Ser Glu Glu Thr Thr Thr Gly Val		
165	170	175
Lys Arg Ser Tyr Gln Met Gln Pro Lys Cys Thr Leu Leu Leu His Ala		
180	185	190
Thr Asp Val Cys Asp Thr Val Ile Lys Ser Lys Ile Asp Asn Leu Tyr		
195	200	205
Gly Cys Arg His Ser Leu Ser Asp Gly Leu Met Arg Ala Thr Asp Val		
210	215	220
Arg Arg Pro Cys Lys Val Ala Leu Val Gly Gly Tyr Gly Asp Val Phe		
225	230	235
240		
Lys Gly Trp Val Ala Ala Leu Lys Gln Ala Gly Ala Arg Val Ile Val		
245	250	255
Thr Glu Ile Pro Gln Ile Cys Ala Val Gln Ala Thr Met Glu Gly Ser		
260	265	270
Ser Val Leu Thr Leu Glu Asp Val Val Ser Asp Val Asp Arg Phe Val		
275	280	285
Thr Thr Thr Gly Asn Lys Asp Leu Ile Met Val Asp His Met Arg Arg		
290	295	300
Met Lys Asn Gln Ala Ile Val Cys Asn Ile Arg Arg Phe Asp Asn Glu		
305	310	315
320		
Ile Asp Met Arg Ser Leu Glu Thr Phe Pro Gly Val Lys Arg Ile Thr		
325	330	335
Ile Lys Ala Gln Thr Asp Arg Trp Val Phe Arg Asp Thr Asn Arg Gly		
340	345	350
Ile Ile Val Pro Ala Glu Gly Arg Leu Met Thr Met Gly Cys Ala Thr		
355	360	365
Gly His Pro Ser Phe Arg Thr Ser Cys Ser Phe Thr Asn Gln Val Ser		
370	375	380
Ser Gln Leu Glu Leu Trp Arg Glu Lys Ser Thr Gly Lys Tyr Glu Lys		
385	390	395
400		
Lys Val Tyr Val Phe Pro Lys His Leu Glu Lys Lys Val Ala Ala Leu		

405

410

415

His Leu Val Lys Leu Gly Ala Arg Leu Thr Lys Leu Ser Arg Cys Thr
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1	5	10	15													

gac	gtc	gat	gaa	att	gtc	agg	tta	agg	aag	agg	ttt	ttc	aag	ttg	gac	96
Asp	Val	Asp	Glu	Ile	Val	Arg	Leu	Arg	Lys	Arg	Phe	Phe	Lys	Leu	Asp	
20	25	30														

aga	gat	tgt	tca	gga	tca	gaa	ctt	gga	agt	gag	ttc	atg	agt	ttg	cct	144
Arg	Asp	Cys	Ser	Gly	Ser	Glu	Leu	Gly	Ser	Glu	Phe	Met	Ser	Leu	Pro	
35	40	45														

caa	gtt	agt	tgc	aac	cct	ctt	cgg	atg	cgt	gag	atg	cgt	aat	ttc	gat	192
Gln	Val	Ser	Ser	Asn	Pro	Leu	Arg	Met	Arg	Glu	Met	Arg	Asn	Phe	Asp	
50	55	60														

aat	gat	tgc	gta	ggg	agt	gtg	gat	ttt	atc	gag	ttc	atc	aat	gga	cgt	240
Asn	Asp	Cys	Val	Gly	Ser	Val	Asp	Phe	Ile	Glu	Phe	Ile	Asn	Gly	Arg	
65	70	75	80													

tcc	agt	ttc	agt	act	gtc	ggg	cag	aag	aat	gct	aaa	ttg	aga	ttt	gca	288
Ser	Ser	Phe	Ser	Thr	Val	Gly	Gln	Lys	Asn	Ala	Lys	Leu	Arg	Phe	Ala	
85	90	95														

ccg	att	atc	tat	gat	tgc	gat	aaa	gat	gga	cct	ata	tca	aac	ggc	gag	336
Pro	Ile	Ile	Tyr	Asp	Cys	Asp	Lys	Asp	Gly	Pro	Ile	Ser	Asn	Gly	Glu	
100	105	110														

tta	ttt	agg	gtg	ttg	cgt	att	atg	gtt	cat	gac	aat	ctg	agt	gat	aat	384
Leu	Phe	Arg	Val	Leu	Arg	Ile	Met	Val	His	Asp	Asn	Leu	Ser	Asp	Asn	
115	120	125														

cag	ctg	cag	cag	cgt	tgc	gat	tgc	acg	cgt	agt	ggc	gga	gat	aat	gac	432
Gln	Leu	Gln	Gln	Arg	Cys	Asp	Cys	Thr	Arg	Ser	Gly	Gly	Asp	Asn	Asp	

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145	150	155	160
ttg cca gct acc gta cgt cgg cgt ccg tac cgt acg ttg gta agc ggt 528 Leu Pro Ala Thr Val Arg Arg Arg Pro Tyr Arg Thr Leu Val Ser Gly			
165	170	175	
gat gtg taa agttcagtgc accgtgaccg tgagcctgga agcctgaacg 577 Asp Val			
ctgacaagcc cttaagccaa aaaattggct gaggcctgat gccctgagat gccaaaggct 637			
ttttaggctt ttagagaaaa aggctaaaaa aaaggctaga aaaaaaggct cttaggcctg 697			
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Arg Asp Cys Ser Gly Ser Glu Leu Gly Ser Glu Phe Met Ser Leu Pro			
35	40	45	
Gln Val Ser Ser Asn Pro Leu Arg Met Arg Glu Met Arg Asn Phe Asp			
50	55	60	
Asn Asp Cys Val Gly Ser Val Asp Phe Ile Glu Phe Ile Asn Gly Arg			
65	70	75	80
Ser Ser Phe Ser Thr Val Gly Gln Lys Asn Ala Lys Leu Arg Phe Ala			
85	90	95	
Pro Ile Ile Tyr Asp Cys Asp Lys Asp Gly Pro Ile Ser Asn Gly Glu			
100	105	110	
Leu Phe Arg Val Leu Arg Ile Met Val His Asp Asn Leu Ser Asp Asn			
115	120	125	
Gln Leu Gln Gln Arg Cys Asp Cys Thr Arg Ser Gly Gly Asp Asn Asp			
130	135	140	
Gly Asp Gly Arg Gly Ala Lys Asn Ser Phe Glu Glu Phe Tyr Gly Arg			
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tgg gcg gtg aac ccc tgc ttc att gct tcc tgt tcc tgt ctc ctc gtt 99
Trp Ala Val Asn Pro Cys Phe Ile Ala Ser Cys Ser Cys Leu Leu Val
   15          20          25          30

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ggc ttc ggc gac gca atc ttc tac gag tcg ttc gcc ggg gat ttt gat    147
Gly Phe Gly Asp Ala Ile Phe Tyr Glu Ser Phe Ala Gly Asp Phe Asp
                         35          40          45

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gca	cgc	tgg	att	tta	tcc	ggc	tca	aag	tgt	ctc	tcg	gat	tcg	gcc	aag	195
Ala	Arg	Trp	Ile	Leu	Ser	Gly	Ser	Lys	Cys	Leu	Ser	Asp	Ser	Ala	Lys	
			50						55					60		

aat gct ggg ttt gat gat tat gga ctt ctt gtg ggt gaa caa gcc agg 243
Asn Ala Gly Phe Asp Asp Tyr Gly Leu Leu Val Gly Glu Gln Ala Arg
65 70 75

aag cct cct ata gtc aag gaa ctt gcc gag tct ctc agt cta aag gac 291
Lys Pro Pro Ile Val Lys Glu Leu Ala Glu Ser Leu Ser Leu Lys Asp
80 85 90

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gga aga gtt gtt ctt gag tgt gag act cgc ctt gac cat ggc atc gac 339
Gly Arg Val Val Leu Glu Cys Glu Thr Arg Leu Asp His Gly Ile Asp
    95           100           105           110

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tgt gga ggt ccc tgt att aga tat ctt cga acc cag gag agc gga tgg 387
 Cys Gly Gly Pro Cys Ile Arg Tyr Leu Arg Thr Gln Glu Ser Gly Trp
 115 120 125

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aaa ttt gac agc tcc acc atg ttt ggt gct gct aag tat ggc gcg agg 435
Lys Phe Asp Ser Ser Thr Met Phe Gly Ala Ala Lys Tyr Gly Ala Arg
          130           135           140

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agg acc cag ttc ttc ggg ggc cac ccc cag aac cca aac agt ggt gag 483
Arg Thr Gln Phe Phe Gly Gly His Pro Gln Asn Pro Asn Ser Gly Glu
145 150 155

tgt gtt gac cat gat cac aac cag cgg gct tcc ctc aca tcg gac aaa	531		
Cys Val Asp His Asp His Asn Gln Arg Ala Ser Leu Thr Ser Asp Lys			
160	165	170	
gta cct cgt ttg tac act gga att ctg tcg ccc gaa aat gaa ttc cag	579		
Val Pro Arg Leu Tyr Thr Gly Ile Leu Ser Pro Glu Asn Glu Phe Gln			
175	180	185	190
atc ttg ata gat cgg ggg ttg gag acc aag gcc aaa atc ttc cct tgt	627		
Ile Leu Ile Asp Arg Gly Leu Glu Thr Lys Ala Lys Ile Phe Pro Cys			
195	200	205	
gag gac ttt gag cct cct gtt ata cca tcc aag aga agc cct gat aat	675		
Glu Asp Phe Glu Pro Pro Val Ile Pro Ser Lys Arg Ser Pro Asp Asn			
210	215	220	
ccg tcg aag cgg act gag gac tcg gac gaa aaa gcc aaa atc cca ggc	723		
Pro Ser Lys Arg Thr Glu Asp Ser Asp Glu Lys Ala Lys Ile Pro Gly			
225	230	235	
cca agt gcc ctg aag cga cag gaa agc gat gag gat ccg aac cgg gaa	771		
Pro Ser Ala Leu Lys Arg Gln Glu Ser Asp Glu Asp Pro Asn Arg Glu			
240	245	250	
atc tta cat gaa gaa gcc ggg aga cgt tcg tcc gat gtt ggg gcc cac	819		
Ile Leu His Glu Ala Gly Arg Arg Ser Ser Asp Val Gly Ala His			
255	260	265	270
gca aaa gac cag gca cac gaa cct gag cca aaa cac tgg ggt gct gaa	867		
Ala Lys Asp Gln Ala His Glu Pro Glu Pro Lys His Trp Gly Ala Glu			
275	280	285	
aag gat ggt gaa tgc gca ccc cca aag att gaa aac gca aag cgg ggg	915		
Lys Asp Gly Glu Cys Ala Pro Pro Lys Ile Glu Asn Ala Lys Arg Gly			
290	295	300	
gcc gcc cct agt tgt ggt gta tcg gag agg caa acc aag att agt cca	963		
Ala Ala Pro Ser Cys Gly Val Ser Glu Arg Gln Thr Lys Ile Ser Pro			
305	310	315	
aat tat aag gga aaa ccc tcc gtg ggt cca aac gtt tac caa ggg att	1011		
Asn Tyr Lys Gly Lys Pro Ser Val Gly Pro Asn Val Tyr Gln Gly Ile			
320	325	330	
tgg aaa ccc cgc gag atg cta aac cct gga tcg ttc caa atc gca aaa	1059		
Trp Lys Pro Arg Glu Met Leu Asn Pro Gly Ser Phe Gln Ile Ala Lys			
335	340	345	350
ccc gct tgt gag cct att gct ggt ata ggc atg gag att agg aag cag	1107		
Pro Ala Cys Glu Pro Ile Ala Gly Ile Gly Met Glu Ile Arg Lys Gln			
355	360	365	
ggc atc cta tta gac act gtg gtg ggg gtt agg ggg gat aca ggt gaa	1155		
Gly Ile Leu Leu Asp Thr Val Val Gly Val Arg Gly Asp Thr Gly Glu			
370	375	380	

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agt ttg cag gct caa gag gcg aga acc ccg tca gac gct ggt tca ccc Ser Leu Gln Ala Gln Glu Ala Arg Thr Arg Ser Asp Ala Gly Ser Pro 400 405 410	1251
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gga acc caa gac cga cga aaa cag gat gtt ggc cga cgc caa gct gcc Gly Thr Gln Asp Arg Arg Lys Gln Asp Val Gly Arg Arg Gln Ala Ala 495 500 505 510	1539
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Trp Ile Leu Ser Gly Ser Lys Cys Leu Ser Asp Ser Ala Lys Asn Ala 50 55 60	

Gly Phe Asp Asp Tyr Gly Leu Leu Val Gly Glu Gln Ala Arg Lys Pro
65 70 75 80

Pro Ile Val Lys Glu Leu Ala Glu Ser Leu Ser Leu Lys Asp Gly Arg
85 90 95

Val Val Leu Glu Cys Glu Thr Arg Leu Asp His Gly Ile Asp Cys Gly
100 105 110

Gly Pro Cys Ile Arg Tyr Leu Arg Thr Gln Glu Ser Gly Trp Lys Phe
115 120 125

Asp Ser Ser Thr Met Phe Gly Ala Ala Lys Tyr Gly Ala Arg Arg Thr
130 135 140

Gln Phe Phe Gly Gly His Pro Gln Asn Pro Asn Ser Gly Glu Cys Val
145 150 155 160

Asp His Asp His Asn Gln Arg Ala Ser Leu Thr Ser Asp Lys Val Pro
165 170 175

Arg Leu Tyr Thr Gly Ile Leu Ser Pro Glu Asn Glu Phe Gln Ile Leu
180 185 190

Ile Asp Arg Gly Leu Glu Thr Lys Ala Lys Ile Phe Pro Cys Glu Asp
195 200 205

Phe Glu Pro Pro Val Ile Pro Ser Lys Arg Ser Pro Asp Asn Pro Ser
210 215 220

Lys Arg Thr Glu Asp Ser Asp Glu Lys Ala Lys Ile Pro Gly Pro Ser
225 230 235 240

Ala Leu Lys Arg Gln Glu Ser Asp Glu Asp Pro Asn Arg Glu Ile Leu
245 250 255

His Glu Glu Ala Gly Arg Arg Ser Ser Asp Val Gly Ala His Ala Lys
260 265 270

Asp Gln Ala His Glu Pro Glu Pro Lys His Trp Gly Ala Glu Lys Asp
275 280 285

Gly Glu Cys Ala Pro Pro Lys Ile Glu Asn Ala Lys Arg Gly Ala Ala
290 295 300

Pro Ser Cys Gly Val Ser Glu Arg Gln Thr Lys Ile Ser Pro Asn Tyr
305 310 315 320

Lys Gly Lys Pro Ser Val Gly Pro Asn Val Tyr Gln Gly Ile Trp Lys
325 330 335

Pro Arg Glu Met Leu Asn Pro Gly Ser Phe Gln Ile Ala Lys Pro Ala
340 345 350

Cys Glu Pro Ile Ala Gly Ile Gly Met Glu Ile Arg Lys Gln Gly Ile
355 360 365

Leu Leu Asp Thr Val Val Gly Val Arg Gly Asp Thr Gly Glu Glu Tyr
 370 375 380
 Gly Glu Thr Pro Leu Lys Thr Thr Cys Thr Val Glu Lys His Ser Leu
 385 390 395 400
 Gln Ala Gln Glu Ala Arg Thr Arg Ser Asp Ala Gly Ser Pro Tyr Thr
 405 410 415
 Arg Tyr Val Ser Lys Ile Pro Gly Lys Ala Asp Asn Pro Phe Ser Ser
 420 425 430
 Glu His Lys Cys Lys Asn Phe Asp Leu Ile Glu Ala Glu Lys Gln Cys
 435 440 445
 Ala Asn Ala Val Ile Leu Gly Val Val Val Asn Ser Gly Ser Ile Asn
 450 455 460
 Ser Val Val Ser Trp Gly Tyr Lys Pro Gly Thr Val Asn Lys Asn Gln
 465 470 475 480
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 485 490 495
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 Arg Val Thr Arg Asp Gly Ser Gly Pro Gly Lys Thr Gly Val Thr Arg
 15 20 25
 ggg tcg tca ccc atg cga tgg gca tgg aag cgg tgg caa gcc gtc ggg 147
 Gly Ser Ser Pro Met Arg Trp Ala Trp Lys Arg Trp Gln Ala Val Gly
 30 35 40 45
 gca tcg acg gcc cgc acg tgg ttc ggg aca gag aac cag aaa gga ata 195
 Ala Ser Thr Ala Arg Thr Trp Phe Gly Thr Glu Asn Gln Lys Gly Ile
 50 55 60

///

acg aca agc acc cgc gcg cgg cgc tac gcg gtc tcg gcc aaa ttc ccg	243
Thr Thr Ser Thr Arg Ala Arg Arg Tyr Ala Val Ser Ala Lys Phe Pro	
65	70
75	
aga tta agt aat aag ggc aaa gat tac atg cgt tgc gtc ctc caa tac	291
Arg Leu Ser Asn Lys Gly Lys Asp Tyr Met Arg Cys Val Leu Gln Tyr	
80	85
90	
acc gtc aaa aat gaa caa aaa gtt gat tgt ggt ggc tca tat atc aag	339
Thr Val Lys Asn Glu Gln Lys Val Asp Cys Gly Gly Ser Tyr Ile Lys	
95	100
105	
tta tta cct tcg aaa ttg cgc acg ggt gat ggt gat ggc gtg tca gaa	387
Leu Leu Pro Ser Lys Leu Arg Thr Gly Asp Gly Asp Gly Val Ser Glu	
110	115
120	125
tat tca att atg ttt ggt cca gat tcg aca ggt gca tca cgt act gtt	435
Tyr Ser Ile Met Phe Gly Pro Asp Ser Thr Gly Ala Ser Arg Thr Val	
130	135
140	
cgt cga gct cgc aat tat aag ggt aaa cgg cat ttg cgg aaa aaa gaa	483
Arg Arg Ala Arg Asn Tyr Lys Gly Lys Arg His Leu Arg Lys Lys Glu	
145	150
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cag aat aaa gtg gaa aca gat caa tta aca cat cag tat act acg agt	531
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Trp Ser Pro Asp Trp Thr Tyr Asn Val Leu Val Asp Asn Lys Glu Ser	
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Gln Ala Gly Asn Leu Ala Asp Asp Cys Glu Leu Leu Pro Gln Lys Arg	
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Ile Phe Arg Pro Ser Cys Arg Lys Gln Ser Lys Pro Val Thr Cys Val	
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Arg Pro Arg Arg Tyr Lys Gly Glu Thr Lys Ala Lys Lys His Pro Arg	
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345

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Gln Lys Gln Ile Gln Ser Ala Gly Lys Arg Gly Phe Phe Tyr Ser Lys		
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Lys Ser Ser Gly Ser Asn Val Arg Glu Arg Phe Thr Phe Glu Asp Met		
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Leu Cys Phe Gln Lys Asn Met Ser Leu Ser Pro Ser Phe Leu Gln Asp		
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Pro Ile Pro Thr Ser Leu Leu Lys Ile Asn Ser Asp Leu Val Ser Arg		
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Ala Thr Lys Leu Phe His Leu Ile Leu Lys Tyr Met Gly Val Asp Ser		
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Ser Asp Arg Ser Thr Pro Pro Ser Leu Asp Glu Arg Ile Asp Leu Val		
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Gly Lys Leu Phe Lys Lys Thr Leu Lys Arg Val Glu Leu Arg Asp Glu		
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Leu Phe Ala Gln Ile Ser Lys Gln Thr Arg His Asn Pro Asp Arg Gln		
195	200	205
Tyr Leu Ile Lys Ala Trp Glu Leu Met Tyr Leu Cys Ala Ser Ser Met		
210	215	220
Pro Pro Ser Lys Asp Ile Gly Gly Tyr Leu Ser Glu Tyr Ile His Asn		
225	230	235
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Val Ala His Asp Ala Thr Ile Glu Pro Asp Ala Gln Val Leu Ala Val		
245	250	255
Asn Thr Leu Lys Ala Leu Lys Arg Ser Ile Lys Ala Gly Pro Arg His		
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Thr Thr Pro Gly Arg Glu Glu Ile Glu Ala Leu Leu Thr Gly Arg Lys		
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Leu Thr Thr Ile Val Phe Phe Leu Asp Glu Thr Phe Glu Glu Ile Ser		
290	295	300
Tyr Asp Met Ala Thr Thr Val Ser Asp Ala Val Glu Leu Ala Gly Thr		
305	310	315
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Ile Lys Leu Ser Ala Phe Ser Ser Phe Ser Leu Phe Glu Cys Arg Lys		
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Val Val Ser Ser Ser Lys Ser Ser Asp Pro Gly Asn Glu Glu Tyr Ile		

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Gly Leu Asp Asp Asn Lys Tyr Ile Gly Asp Leu Leu Ala Glu Phe Lys		
355	360	365
Ala Ile Lys Asp Arg Asn Lys Gly Glu Ile Leu His Cys Lys Leu Val		
370	375	380
Phe Lys Lys Lys Leu Phe Arg Glu Ser Asp Glu Ala Val Thr Asp Leu		
385	390	395
Met Phe Val Gln Leu Ser Tyr Val Gln Leu Gln His Asp Tyr Leu Leu		
405	410	415
Gly Asn Tyr Pro Val Gly Arg Asp Asp Ala Ala Gln Leu Cys Ala Leu		
420	425	430
Gln Ile Leu Val Gly Ile Gly Phe Val Asn Ser Pro Glu Ser Cys Ile		
435	440	445
Asp Trp Thr Ser Leu Leu Glu Arg Phe Leu Pro Arg Gln Ile Ala Ile		
450	455	460
Thr Arg Ala Lys Arg Glu Trp Glu Leu Asp Ile Leu Ala Arg Tyr Arg		
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Arg Tyr Arg Gln Gln Phe Leu Arg Ser Val Pro Asp Ala Leu Leu Val		
485	490	495
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Lys Ile Asp Asp Pro Ile Gly Leu Leu Pro Gly Arg Ile Ile Leu Gly		
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Ile Asn Lys Arg Gly Val His Phe Phe Arg Pro Val Pro Lys Glu Tyr		
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Leu His Ser Ala Glu Leu Arg Asp Ile Met Gln Phe Gly Ser Ser Asn		
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Thr Ala Val Phe Phe Lys Met Arg Val Ala Gly Val Leu His Ile Phe		
565	570	575
Gln Phe Glu Thr Lys Gln Gly Glu Glu Ile Cys Val Ala Leu Gln Thr		
580	585	590
His Ile Asn Asp Val Met Leu Arg Arg Tyr Ser Lys Ala Arg Ser Ala		
595	600	605
Ala Asn Cys Leu Val Asn Gly Asp Ile Ser Cys Cys Ser Lys Pro Gln		
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Asn Phe Glu Val Tyr Glu Lys Arg Leu Gln Asp Leu Ser Lys Ala Tyr		
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Glu Glu Ser Gln Lys Ile Glu Lys Leu Met Asp Glu Gln Gln Glu		

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Lys Asn Gln Gln Glu Val Thr Leu Arg Glu Glu Leu Glu Ala Ile His			
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Arg Asp Lys Leu Arg Ser Leu Cys Asp Glu Lys Gly Thr Pro Ile Gln			
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Ser Leu Met Ser Glu Leu Arg Gly Met Glu Ala Arg Leu Ala Lys Ser			
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Gly Asn Thr Lys Ser Ser Lys Glu Thr Lys Ser Glu Leu Ala Glu Met			
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Asn Asn Gln Ile Leu Tyr Lys Ile Gln Lys Glu Leu Glu Val Arg Asn			
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Lys Glu Leu His Val Ala Val Asp Asn Ser Lys Arg Leu Leu Ser Glu			
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Glu Val Glu Ile His Gln Lys Arg Tyr Glu Gln Glu Lys Lys Val Leu			
785	790	795	800
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Asp Leu Asp Ser Ala Glu Ser Thr Ile Glu Ser Lys Asn Ser Asp Met			
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Ser Glu Arg Glu Lys Gln Met Leu Thr Thr Val Asp Glu Phe Thr Val			
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Glu His Ala Trp Lys Asp Asp Lys Arg Lys Gln His Ile Tyr Asp Arg			
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Val Phe Asp Met Arg Ala Ser Gln Asp Asp Ile Phe Glu Asp Thr Lys			

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Tyr Leu Val Gln Ser Ala Val Asp Gly Tyr Asn Val Cys Ile Phe Ala			
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Tyr Gly Gln Thr Gly Ser Gly Lys Thr Phe Thr Ile Tyr Gly His Glu			
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Ser Asn Pro Gly Leu Thr Pro Arg Ala Thr Lys Glu Leu Phe Asn Ile			
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Leu Lys Arg Asp Ser Lys Arg Phe Ser Phe Ser Leu Lys Ala Tyr Met			
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Val Glu Leu Tyr Gln Asp Thr Leu Val Asp Leu Leu Leu Pro Lys Ser			
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Ala Arg Arg Leu Lys Leu Glu Ile Lys Lys Asp Ser Lys Gly Met Val			
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Phe Val Glu Asn Val Thr Thr Ile Pro Ile Ser Thr Leu Glu Glu Leu			
1060	1065	1070	
Arg Met Ile Leu Glu Arg Gly Ser Glu Arg Arg His Val Ser Gly Thr			
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Asn Met Asn Glu Glu Ser Ser Arg Ser His Leu Ile Leu Ser Val Val			
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Ile Glu Ser Ile Asp Leu Gln Thr Gln Ser Ala Ala Arg Gly Lys Leu			
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Ser Phe Val Asp Leu Ala Gly Ser Glu Arg Val Lys Lys Ser Gly Ser			
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Ala Gly Cys Gln Leu Lys Glu Ala Gln Ser Ile Asn Lys Ser Leu Ser			
1140	1145	1150	
Ala Leu Gly Asp Val Ile Gly Ala Leu Ser Ser Gly Asn Gln His Ile			
1155	1160	1165	
Pro Tyr Arg Asn His Lys Leu Thr Met Leu Met Ser Asp Ser Leu Gly			
1170	1175	1180	
Gly Asn Ala Lys Thr Leu Met Phe Val Asn Val Ser Pro Ala Glu Ser			
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Asn Leu Asp Glu Thr Tyr Asn Ser Leu Leu Tyr Ala Ser Arg Val Arg			
1205	1210	1215	
Thr Ile Val Asn Asp Pro Ser Lys His Ile Ser Ser Lys Glu Met Val			
1220	1225	1230	
Arg Leu Lys Lys Leu Val Ala Tyr Trp Lys Glu Gln Ala Gly Lys Lys			
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 Val Pro Ile Asn Pro Pro Thr Thr Lys Arg Asp Leu Arg Gln Asn Asp
 20 25 30

aat aat aac cct aag agt cat aat agt cat aat agc aat ggg atg act 144
 Asn Asn Asn Pro Lys Ser His Asn Ser His Asn Ser Asn Gly Met Thr
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 Gly Asn Arg Asn Asn Asn Lys Asn Ala Gly Gly Val Glu Thr Ser
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aaa aaa gcg cgc tca cga ctg gaa aca cat ccc cga gat aat gag aat 240
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 Val Asp Val Pro Val Ile Leu Ser Thr Arg Glu Ser Gln Gly Thr Arg
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 Ser Val Asn Ala Thr Ser Lys Ile Arg Cys Pro Asp Ser Thr Ala Ile
 115 120 125

tgc gag tgg ttc gcc acg ccc acg gat cct caa aga cca gga gtt tat 432
 Cys Glu Trp Phe Ala Thr Pro Thr Asp Pro Gln Arg Pro Gly Val Tyr
 130 135 140

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 Asn His Lys Asn Gly Asp Lys Asn Asn Arg Asp Thr Gly Asn Ile Asn
 145 150 155 160

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Thr Val Ser Ser Leu Met Asp Asn Ala Arg Gly Pro Asn Pro Arg Ser	
165	170
	175
ggg att tca ata ccg aca cca acc tct aga caa tcc cca agt gag aca	576
Gly Ile Ser Ile Pro Thr Pro Thr Ser Arg Gln Ser Pro Ser Glu Thr	
180	185
	190
cct cca gat cca ctg cag aat cct aat tat act agg tat cat aat	624
Pro Pro Asp Pro Leu Gln Asn Pro Asn Asn Tyr Thr Arg Tyr His Asn	
195	200
	205
gat aaa aac agc aag aat agt aac aac tac aat aag aga aat aag	672
Asp Lys Asn Ser Lys Asn Ser Asn Arg Asn Tyr Asn Lys Arg Asn Lys	
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aac tcg acg acc ttt aat aac tcg gac ctt cct ggt cat aat aga agc	720
Asn Ser Thr Thr Phe Asn Asn Ser Asp Leu Pro Gly His Asn Arg Ser	
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	235
	240
tcc cct gcg att aat gca gta aaa tca gca tca aat cga tca tct gct	768
Ser Pro Ala Ile Asn Ala Val Lys Ser Ala Ser Asn Arg Ser Ser Ala	
245	250
	255
ata ggt agt cga aac agt gat tta aac aat gct gct aat gat gaa cgc	816
Ile Gly Ser Arg Asn Ser Asp Leu Asn Asn Ala Ala Asn Asp Glu Arg	
260	265
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cat tac gct aga tcg gga aca tat cag ata aac gct gta aca gta ctt	864
His Tyr Ala Arg Ser Gly Thr Tyr Gln Ile Asn Ala Val Thr Val Leu	
275	280
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aga gta tta gga aga gga gca cgg cgt gat gta aag tca gca tat cat	912
Arg Val Leu Gly Arg Gly Ala Arg Arg Asp Val Lys Ser Ala Tyr His	
290	295
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ggc acc tgt ggt aca ggt ccc cgg atg aaa gtg ata aca ttg gct gtt	960
Gly Thr Cys Gly Thr Gly Pro Arg Met Lys Val Ile Thr Leu Ala Val	
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caa gag aat att aga aac cga att ata ttg gag cta cgg aca tta cac	1008
Gln Glu Asn Ile Arg Asn Arg Ile Ile Leu Glu Leu Arg Thr Leu His	
325	330
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aag acc tct tat caa tat atc gtt ccg tat tat gat ggg atc tat aca	1056
Lys Thr Ser Tyr Gln Tyr Ile Val Pro Tyr Tyr Asp Gly Ile Tyr Thr	
340	345
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gag ggc tca att ttc att cgg atg gtg gaa ctt gga tgg gta acg aat	1104
Glu Gly Ser Ile Phe Ile Arg Met Val Glu Leu Gly Trp Val Thr Asn	
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atc atg aac aaa acg gcg acc ata cgt gcg ccg gtt ttg ggt acg atg	1152
Ile Met Asn Lys Thr Ala Thr Ile Arg Ala Pro Val Leu Gly Thr Met	
370	375
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Lys Cys Pro Ser Lys Arg Asp Ile Lys Pro Ser Asp Ile Leu Val Asn			
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Asn Glu Gly Arg Ala Lys Ile Ala Gly Phe Gly Val Ser Gly Gln Leu			
420	425	430	
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Gln His Thr Leu Ser Lys Asp Val Thr Ser Val Glu Ser Pro Glu Arg			
435	440	445	
cgt agt ggt agg tct tat ggt ttc gat cga gat att tgg agt gat ggt			1392
Arg Ser Gly Arg Ser Tyr Gly Phe Asp Arg Asp Ile Trp Ser Asp Gly			
450	455	460	
ata aca cgt gta tca tgc gca atc ggg aga ttc cct tat gct tgt aat			1440
Ile Thr Arg Val Ser Cys Ala Ile Gly Arg Phe Pro Tyr Ala Cys Asn			
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tac cca caa cag ctc cca caa gca tca caa cac cag cta cag caa cag			1488
Tyr Pro Gln Gln Leu Pro Gln Ala Ser Gln His Gln Leu Gln Gln Gln			
485	490	495	
caa caa aaa cga ccg gcg tta caa cca aag caa gaa caa ccg gaa gta			1536
Gln Gln Lys Arg Pro Ala Leu Gln Pro Lys Gln Glu Gln Pro Glu Val			
500	505	510	
gag aaa cac cga tta caa ata cca cgt caa aat tta gct gta tat aat			1584
Glu Lys His Arg Leu Gln Ile Pro Arg Gln Asn Leu Ala Val Tyr Asn			
515	520	525	
agt aat cac gat ata tgg aat aat cgc aat aga gat aaa tat att att			1632
Ser Asn His Asp Ile Trp Asn Asn Arg Asn Arg Asp Lys Tyr Ile Ile			
530	535	540	
agt aac aat cct aat aat agg aat gat aat aat aac act gta tgc gat			1680
Ser Asn Asn Pro Asn Asn Arg Asn Asp Asn Asn Asn Thr Val Cys Asp			
545	550	555	560
cta agc agt ggc gag tta ggt gaa agt cgt gag gtt gtg cca gac ggt			1728
Leu Ser Ser Gly Glu Leu Gly Glu Ser Arg Glu Val Val Pro Asp Gly			
565	570	575	
atc ggg ttg gag gta ctt cta gat tct atc gta aaa gaa gag gta cga			1776
Ile Gly Leu Glu Val Leu Leu Asp Ser Ile Val Lys Glu Glu Val Arg			
580	585	590	
atg gaa cca tca aca gtt tcg aag gaa ttt agg tcg atc att tct gaa			1824
Met Glu Pro Ser Thr Val Ser Lys Glu Phe Arg Ser Ile Ile Ser Glu			
595	600	605	
tgt tta cga aac gat gca act gaa aga caa aca gct tca aac tta gta			1872
Cys Leu Arg Asn Asp Ala Thr Glu Arg Gln Thr Ala Ser Asn Leu Val			

610	615	620	
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acc gca gat tta caa agg tgg caa taa aaatgcctt cacgcctgat Thr Ala Asp Leu Gln Arg Trp Gln 645			1967
cgctgacgct cgacgcctgc ccccagcctg cagctcgccc agctcgccca ggctcgccca gcctgcccac cagcctgccc caccgctcca cgcctaaata ataaaaattt ttaaaaaaaaa aaaaaaaaaa aaaccgct			2027 2087 2105
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Lys Lys Ala Arg Ser Arg Leu Glu Thr His Pro Arg Asp Asn Glu Asn 65 70 75 80			
Asn Tyr Arg Leu Ala Thr Ser Ala Gly Thr Lys Gly Gly Ala Arg Thr 85 90 95			
Val Asp Val Pro Val Ile Leu Ser Thr Arg Glu Ser Gln Gly Thr Arg 100 105 110			
Ser Val Asn Ala Thr Ser Lys Ile Arg Cys Pro Asp Ser Thr Ala Ile 115 120 125			
Cys Glu Trp Phe Ala Thr Pro Thr Asp Pro Gln Arg Pro Gly Val Tyr 130 135 140			
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Thr Val Ser Ser Leu Met Asp Asn Ala Arg Gly Pro Asn Pro Arg Ser 165 170 175			
Gly Ile Ser Ile Pro Thr Pro Thr Ser Arg Gln Ser Pro Ser Glu Thr			

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Pro Pro Asp Pro Leu Gln Asn Pro Asn Asn Tyr Thr Arg Tyr His Asn		
195	200	205
Asp Lys Asn Ser Lys Asn Ser Asn Arg Asn Tyr Asn Lys Arg Asn Lys		
210	215	220
Asn Ser Thr Thr Phe Asn Asn Ser Asp Leu Pro Gly His Asn Arg Ser		
225	230	235
Ser Pro Ala Ile Asn Ala Val Lys Ser Ala Ser Asn Arg Ser Ser Ala		
245	250	255
Ile Gly Ser Arg Asn Ser Asp Leu Asn Asn Ala Ala Asn Asp Glu Arg		
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His Tyr Ala Arg Ser Gly Thr Tyr Gln Ile Asn Ala Val Thr Val Leu		
275	280	285
Arg Val Leu Gly Arg Gly Ala Arg Arg Asp Val Lys Ser Ala Tyr His		
290	295	300
Gly Thr Cys Gly Thr Gly Pro Arg Met Lys Val Ile Thr Leu Ala Val		
305	310	315
320		
Gln Glu Asn Ile Arg Asn Arg Ile Ile Leu Glu Leu Arg Thr Leu His		
325	330	335
Lys Thr Ser Tyr Gln Tyr Ile Val Pro Tyr Tyr Asp Gly Ile Tyr Thr		
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Glu Gly Ser Ile Phe Ile Arg Met Val Glu Leu Gly Trp Val Thr Asn		
355	360	365
Ile Met Asn Lys Thr Ala Thr Ile Arg Ala Pro Val Leu Gly Thr Met		
370	375	380
Ala Phe Leu Val Leu Gln Gly Arg Ile Tyr Val His Arg Lys Phe Asp		
385	390	395
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Lys Cys Pro Ser Lys Arg Asp Ile Lys Pro Ser Asp Ile Leu Val Asn		
405	410	415
Asn Glu Gly Arg Ala Lys Ile Ala Gly Phe Gly Val Ser Gly Gln Leu		
420	425	430
Gln His Thr Leu Ser Lys Asp Val Thr Ser Val Glu Ser Pro Glu Arg		
435	440	445
Arg Ser Gly Arg Ser Tyr Gly Phe Asp Arg Asp Ile Trp Ser Asp Gly		
450	455	460
Ile Thr Arg Val Ser Cys Ala Ile Gly Arg Phe Pro Tyr Ala Cys Asn		
465	470	475
Tyr Pro Gln Gln Leu Pro Gln Ala Ser Gln His Gln Leu Gln Gln Gln		

485	490	495
Gln Gln Lys Arg Pro Ala Leu Gln Pro Lys Gln Glu Gln Pro Glu Val 500	505	510
Glu Lys His Arg Leu Gln Ile Pro Arg Gln Asn Leu Ala Val Tyr Asn 515	520	525
Ser Asn His Asp Ile Trp Asn Asn Arg Asn Arg Asp Lys Tyr Ile Ile 530	535	540
Ser Asn Asn Pro Asn Asn Arg Asn Asp Asn Asn Asn Thr Val Cys Asp 545	550	555
Leu Ser Ser Gly Glu Leu Gly Glu Ser Arg Glu Val Val Pro Asp Gly 565	570	575
Ile Gly Leu Glu Val Leu Leu Asp Ser Ile Val Lys Glu Glu Val Arg 580	585	590
Met Glu Pro Ser Thr Val Ser Lys Glu Phe Arg Ser Ile Ile Ser Glu 595	600	605
Cys Leu Arg Asn Asp Ala Thr Glu Arg Gln Thr Ala Ser Asn Leu Val 610	615	620
Asn His Glu Phe Val Lys Lys Tyr Gln Lys Tyr Asn Arg Glu Lys Trp 625	630	635
Thr Ala Asp Leu Gln Arg Trp Gln 645		
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Arg Pro Ser Val Phe Cys Ser Ile Pro Gly Leu Gly Gly Asp Ser His		
cga aaa cct cca agt gac ggt ttc ctc aag ctg cct gcg tcg tct att 20	35	40
Arg Lys Pro Pro Ser Asp Gly Phe Leu Lys Leu Pro Ala Ser Ser Ile		
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		196

Pro Ala Asp Ser Arg Lys Leu Val Ala Asn Ser Thr Ser Phe His Pro			
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Ile Ser Ala Val Asn Val Ser Ala Gln Ala Ser Leu Thr Ala Asp Phe			
60	65	70	
ccc gcc ctt tca gaa act ata ctg aaa gag gga aga aat aac gga aaa			292
Pro Ala Leu Ser Glu Thr Ile Leu Lys Glu Gly Arg Asn Asn Gly Lys			
75	80	85	
gag aaa gca gag aac atc gtg tgg cac gag agt tcg ata tgc aga tgc			340
Glu Lys Ala Glu Asn Ile Val Trp His Glu Ser Ser Ile Cys Arg Cys			
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gac aga caa caa ctt ctt caa caa aag ggt tgt gtc gtt tgg atc act			388
Asp Arg Gln Gln Leu Leu Gln Gln Lys Gly Cys Val Val Trp Ile Thr			
110	115	120	
ggt ctc agt ggt tca ggg aaa agc act gtt gct tgt gca cta agt aaa			436
Gly Leu Ser Gly Ser Gly Lys Ser Thr Val Ala Cys Ala Leu Ser Lys			
125	130	135	
gca ttg ttt gaa aga ggc aaa ctt act tac aca ctc gac ggc gac aat			484
Ala Leu Phe Glu Arg Gly Lys Leu Thr Tyr Thr Leu Asp Gly Asp Asn			
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gtc cgt cac ggc ctt aac cgt gac ctc act ttc aaa gca gag cac cgc			532
Val Arg His Gly Leu Asn Arg Asp Leu Thr Phe Lys Ala Glu His Arg			
155	160	165	
acc gaa aac att aga aga att ggt gag gtg gct aag ttg ttt gct gac			580
Thr Glu Asn Ile Arg Arg Ile Gly Glu Val Ala Lys Leu Phe Ala Asp			
170	175	180	185
gtc gga gtc att tgt ata gca agt ttg att tct ccg tac cgg aga gac			628
Val Gly Val Ile Cys Ile Ala Ser Leu Ile Ser Pro Tyr Arg Arg Asp			
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aga gac gcg tgc cgg tcc ttg tta cct gac ggc gat ttc gtc gag gtc			676
Arg Asp Ala Cys Arg Ser Leu Leu Pro Asp Gly Asp Phe Val Glu Val			
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Phe Met Asp Val Pro Leu His Val Cys Glu Ser Arg Asp Pro Lys Gly			
220	225	230	
ttg tac aag ctt gca cgt gca ggc aaa atc aaa ggc ttc act gga atc			772
Leu Tyr Lys Leu Ala Arg Ala Gly Lys Ile Lys Gly Phe Thr Gly Ile			
235	240	245	
gac gac cct tac gag gca cca gtg aat tgc gag gta gtg ctg aaa cac			820
Asp Asp Pro Tyr Glu Ala Pro Val Asn Cys Glu Val Val Leu Lys His			
250	255	260	265
aca gga gac gac gag tcg tgt tcg cca cgt cag atg gct gag aac atc			868
Thr Gly Asp Asp Glu Ser Cys Ser Pro Arg Gln Met Ala Glu Asn Ile			

270	275	280														
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285	290															
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			20					25					30			
Phe	Leu	Lys	Leu	Pro	Ala	Ser	Ser	Ile	Pro	Ala	Asp	Ser	Arg	Lys	Leu	
			35				40					45				
Val	Ala	Asn	Ser	Thr	Ser	Phe	His	Pro	Ile	Ser	Ala	Val	Asn	Val	Ser	
			50				55					60				
Ala	Gln	Ala	Ser	Leu	Thr	Ala	Asp	Phe	Pro	Ala	Leu	Ser	Glu	Thr	Ile	
			65				70				75			80		
Leu	Lys	Glu	Gly	Arg	Asn	Asn	Gly	Lys	Glu	Lys	Ala	Glu	Asn	Ile	Val	
			85				90					95				
Trp	His	Glu	Ser	Ser	Ile	Cys	Arg	Cys	Asp	Arg	Gln	Gln	Leu	Leu	Gln	
			100				105					110				
Gln	Lys	Gly	Cys	Val	Val	Trp	Ile	Thr	Gly	Leu	Ser	Gly	Ser	Gly	Lys	
			115				120					125				
Ser	Thr	Val	Ala	Cys	Ala	Leu	Ser	Lys	Ala	Leu	Phe	Glu	Arg	Gly	Lys	
			130				135				140					
Leu	Thr	Tyr	Thr	Leu	Asp	Gly	Asp	Asn	Val	Arg	His	Gly	Leu	Asn	Arg	
			145				150			155			160			
Asp	Leu	Thr	Phe	Lys	Ala	Glu	His	Arg	Thr	Glu	Asn	Ile	Arg	Arg	Ile	
			165				170					175				
Gly	Glu	Val	Ala	Lys	Leu	Phe	Ala	Asp	Val	Gly	Val	Ile	Cys	Ile	Ala	
			180				185					190				
Ser	Leu	Ile	Ser	Pro	Tyr	Arg	Arg	Asp	Arg	Asp	Ala	Cys	Arg	Ser	Leu	
			195				200					205				
Leu	Pro	Asp	Gly	Asp	Phe	Val	Glu	Val	Phe	Met	Asp	Val	Pro	Leu	His	
			210				215				220					

Val Cys Glu Ser Arg Asp Pro Lys Gly Leu Tyr Lys Leu Ala Arg Ala
 225 230 235 240
 Gly Lys Ile Lys Gly Phe Thr Gly Ile Asp Asp Pro Tyr Glu Ala Pro
 245 250 255
 Val Asn Cys Glu Val Val Leu Lys His Thr Gly Asp Asp Glu Ser Cys
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 Gly Tyr Leu Glu Gly
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 Ser Gly Ala Ser Thr Lys Tyr Asp Ala Lys Asp Ile Gly Ser Leu Gly
 15 20 25

 agc aag gct tcg tct gtg tct gta aga cca agc cct cga act gag ggt 147
 Ser Lys Ala Ser Ser Val Ser Val Arg Pro Ser Pro Arg Thr Glu Gly
 30 35 40 45

 gag atc tta cag tct cca aat ctc aag agt ttt agc ttt gct gag ctt 195
 Glu Ile Leu Gln Ser Pro Asn Leu Lys Ser Phe Ser Phe Ala Glu Leu
 50 55 60

 aaa tca gca acc agg aat ttt aga cca gac agt gtg ctt ggt gaa ggt 243
 Lys Ser Ala Thr Arg Asn Phe Arg Pro Asp Ser Val Leu Gly Glu Gly
 65 70 75

 gga ttc ggt tgt gtt ttc aaa gga tgg att gat gag aag tct ctc act 291
 Gly Phe Gly Cys Val Phe Lys Gly Trp Ile Asp Glu Lys Ser Leu Thr
 80 85 90

 gcc tca aga cca ggc acg ggt ttg gtt att gcc gtc aaa aag ctt aac 339
 Ala Ser Arg Pro Gly Thr Gly Leu Val Ile Ala Val Lys Lys Leu Asn
 95 100 105

 caa gat ggt tgg caa ggt cac cag gag tgg ctg gct gaa gtg aat tac 387
 Gln Asp Gly Trp Gln Gly His Gln Glu Trp Leu Ala Glu Val Asn Tyr

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ctt ggt cag ttt tct cac cgt cac ctt gtg aag ctg att ggt tat tgc Leu Gly Gln Phe Ser His Arg His Leu Val Lys Leu Ile Gly Tyr Cys				435
130 135 140				
cta gag gat gag cac cgt ctt ctt tac gag ttc atg cct cgg ggt Leu Glu Asp Glu His Arg Leu Leu Val Tyr Glu Phe Met Pro Arg Gly				483
145 150 155				
agc ttg gag aat cat ctt ttc agg aga ggt ttg tac ttc caa ccg tta Ser Leu Glu Asn His Leu Phe Arg Arg Gly Leu Tyr Phe Gln Pro Leu				531
160 165 170				
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175 180 185				
gct ttt ctt cac agt tcc gag aca aga gtg ata tac cga gat ttc aag Ala Phe Leu His Ser Ser Glu Thr Arg Val Ile Tyr Arg Asp Phe Lys				627
190 195 200 205				
act tct aat atc ctt ctt gac tcg gag tac aac gca aag ctt tct gat Thr Ser Asn Ile Leu Leu Asp Ser Glu Tyr Asn Ala Lys Leu Ser Asp				675
210 215 220				
ttt ggg ttg gct aag gat ggg cca ata ggt gat aaa agt cat gtc tct Phe Gly Leu Ala Lys Asp Gly Pro Ile Gly Asp Lys Ser His Val Ser				723
225 230 235				
aca cga gtc atg ggt aca cac gga tat gca gct cct gaa tac ctt gca Thr Arg Val Met Gly Thr His Gly Tyr Ala Ala Pro Glu Tyr Leu Ala				771
240 245 250				
acc ggt cat cta aca aca aag agt gat gtc tat agc ttc ggg gtt gtc Thr Gly His Leu Thr Thr Lys Ser Asp Val Tyr Ser Phe Gly Val Val				819
255 260 265				
ctt ctg gag ctg ttg tct ggt cgt cga gca gtg gac aag aac cgc cca Leu Leu Glu Leu Leu Ser Gly Arg Arg Ala Val Asp Lys Asn Arg Pro				867
270 275 280 285				
tct gga gag agg aac ctt gtg gag tgg gct aaa cca tac ctc gta aac Ser Gly Glu Arg Asn Leu Val Glu Trp Ala Lys Pro Tyr Leu Val Asn				915
290 295 300				
aaa aga aag ata ttc cga gtc att gat aat cgt ctt cag gac cag tac Lys Arg Lys Ile Phe Arg Val Ile Asp Asn Arg Leu Gln Asp Gln Tyr				963
305 310 315				
tct atg gaa gaa gca tgt aaa gtg gct act ctg tct ctg aga tgt ctc Ser Met Glu Glu Ala Cys Lys Val Ala Thr Leu Ser Leu Arg Cys Leu				1011
320 325 330				
acc aca gag att aag ctg aga cca aac atg agc gag gtt gtt tcg cac Thr Thr Glu Ile Lys Leu Arg Pro Asn Met Ser Glu Val Val Ser His				1059
335 340 345				

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 Leu Glu His Ile Gln Ser Leu Asn Ala Ala Ile Gly Gly Asn Met Asp
 350 355 360 365

 aaa aca gat aga aga atg cgt agg aga agt gac agt gtt gtc agc aaa 1155
 Lys Thr Asp Arg Arg Met Arg Arg Ser Asp Ser Val Val Ser Lys
 370 375 380

 aaa gtg aat gca ggt ttt gct cga cag act gct gtt ggc agt aca gtt 1203
 Lys Val Asn Ala Gly Phe Ala Arg Gln Thr Ala Val Gly Ser Thr Val
 385 390 395

 gtt gct tat cct cgc cca tca gcc tcg cca ctg tat gtt tga 1245
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 35 40 45

 Gln Ser Pro Asn Leu Lys Ser Phe Ser Phe Ala Glu Leu Lys Ser Ala
 50 55 60

 Thr Arg Asn Phe Arg Pro Asp Ser Val Leu Gly Glu Gly Phe Gly
 65 70 75 80

 Cys Val Phe Lys Gly Trp Ile Asp Glu Lys Ser Leu Thr Ala Ser Arg
 85 90 95

 Pro Gly Thr Gly Leu Val Ile Ala Val Lys Lys Leu Asn Gln Asp Gly
 100 105 110

 Trp Gln Gly His Gln Glu Trp Leu Ala Glu Val Asn Tyr Leu Gly Gln
 115 120 125

 Phe Ser His Arg His Leu Val Lys Leu Ile Gly Tyr Cys Leu Glu Asp
 130 135 140

 Glu His Arg Leu Leu Val Tyr Glu Phe Met Pro Arg Gly Ser Leu Glu
 145 150 155 160

 Asn His Leu Phe Arg Arg Gly Leu Tyr Phe Gln Pro Leu Ser Trp Lys

165	170	175
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His Ser Ser Glu Thr Arg Val Ile Tyr Arg Asp Phe Lys Thr Ser Asn		
195	200	205
Ile Leu Leu Asp Ser Glu Tyr Asn Ala Lys Leu Ser Asp Phe Gly Leu		
210	215	220
Ala Lys Asp Gly Pro Ile Gly Asp Lys Ser His Val Ser Thr Arg Val		
225	230	235
Met Gly Thr His Gly Tyr Ala Ala Pro Glu Tyr Leu Ala Thr Gly His		
245	250	255
Leu Thr Thr Lys Ser Asp Val Tyr Ser Phe Gly Val Val Leu Leu Glu		
260	265	270
Leu Leu Ser Gly Arg Arg Ala Val Asp Lys Asn Arg Pro Ser Gly Glu		
275	280	285
Arg Asn Leu Val Glu Trp Ala Lys Pro Tyr Leu Val Asn Lys Arg Lys		
290	295	300
Ile Phe Arg Val Ile Asp Asn Arg Leu Gln Asp Gln Tyr Ser Met Glu		
305	310	315
Glu Ala Cys Lys Val Ala Thr Leu Ser Leu Arg Cys Leu Thr Thr Glu		
325	330	335
Ile Lys Leu Arg Pro Asn Met Ser Glu Val Val Ser His Leu Glu His		
340	345	350
Ile Gln Ser Leu Asn Ala Ala Ile Gly Gly Asn Met Asp Lys Thr Asp		
355	360	
Arg Arg Met Arg Arg Ser Asp Ser Val Val Ser Lys Lys Val Asn		
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Met Leu Glu Lys Lys Leu Ala Ala Ala Glu Val Ser Glu Glu
1 5 10

gag caa aat aac ttg cta aag gat ttg gag atg aag gaa act gaa tat 158
Glu Gln Asn Asn Leu Leu Lys Asp Leu Glu Met Lys Glu Thr Glu Tyr
15 20 25 30

atg cgc cgt cag agg cat aaa atg gga gct gat gac ttt gag cca ttg 206

Met Arg Arg Gln Arg His Lys Met Gly Ala Asp Asp Phe Glu Pro Leu			
35	40	45	
aca atg att ggg aag ggt gca ttc gga gag gtaacatctc ttttatagat			256
Thr Met Ile Gly Lys Gly Ala Phe Gly Glu			
50	55		
catagtctgt tactctgttt tctcagccctc tcattggcat gcatcatctt gaaatgttct			316
ctgtgatgca tccttcttga aaggcttct taggccattt tttttaccac agctaatttt			376
tcaaaaaagt atggcatgct aattttctc tttctcttg cag gtt agg atc tgt			431
Val Arg Ile Cys			
60			
agg gag aag gga aca ggc aat gtc tat gca atg aag aag ctt aag aaa			479
Arg Glu Lys Gly Thr Gly Asn Val Tyr Ala Met Lys Lys Leu Lys Lys			
65	70	75	
tct gag atg ctt cgc aga ggc cag gta tttaaattcc ttcaagtggc			526
Ser Glu Met Leu Arg Arg Gly Gln Val			
80	85		
tttcgtttga catttgttta gttggttgat gtgaatgtgg aatctgattt tcag gtg			583
Val			
gaa cat gta aaa gca gag aga aat tta ctt gca gaa gtt gat agc aat			631
Glu His Val Lys Ala Glu Arg Asn Leu Leu Ala Glu Val Asp Ser Asn			
90	95	100	
tgc att gtc aaa ctg tat tgt tct ttc caa gat gaa gag tac ttg tat			679
Cys Ile Val Lys Leu Tyr Cys Ser Phe Gln Asp Glu Glu Tyr Leu Tyr			
105	110	115	
ctc ata atg gag tat tta cct ggt ggg gat atg atg act tta ctt atg			727
Leu Ile Met Glu Tyr Leu Pro Gly Gly Asp Met Met Thr Leu Leu Met			
120	125	130	
agg aaa gac acc ctc act gaa gac gag gcc agg ttt tat att ggg gaa			775
Arg Lys Asp Thr Leu Thr Glu Asp Glu Ala Arg Phe Tyr Ile Gly Glu			
135	140	145	150
act gtc ctg gct att gag tcc att cat aag cac aac tac att cac ag			822
Thr Val Leu Ala Ile Glu Ser Ile His Lys His Asn Tyr Ile His Ar			
155	160	165	
gtcagtgaag cagaatatat gat tagtccat tgttatccc ttctaaacgt			882
cttttttct ccaatgtgat acag a gat atc aag cct gat aat ctg cta ctt			934
g Asp Ile Lys Pro Asp Asn Leu Leu Leu			
s	170	175	
gac aaa gac ggc cac atg aaa ttg tca gat ttt gga tta tgt aaa cca			982
Asp Lys Asp Gly His Met Lys Leu Ser Asp Phe Gly Leu Cys Lys Pro			
180	185	190	
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Leu Asp Cys Ser Asn Leu Gln Glu Asp Phe Thr Val Ala Arg Asn
 195 200 205
 gtt agt ggg gct tta caa agt gat ggt cgc cct gtg gcg aca aga cgc 1078
 Val Ser Gly Ala Leu Gln Ser Asp Gly Arg Pro Val Ala Thr Arg Arg
 210 215 220
 acc caa caa gag caa tta cta aac tgg cag aga aat aga agg atg ctt 1126
 Thr Gln Gln Glu Gln Leu Leu Asn Trp Gln Arg Asn Arg Arg Met Leu
 225 230 235
 gtaagttca ctatttcctc atctttctt ccagagatgt ggagtagtcc acagtatcca 1186
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 Ala Tyr Ser Thr Val Gly Thr Pro
 240 245
 gac tat att gcc cca gaa gtt ctg ttg aaa aaa gga tat gga atg gaa 1347
 Asp Tyr Ile Ala Pro Glu Val Leu Leu Lys Lys Gly Tyr Gly Met Glu
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 Cys Asp Tr
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 atg tat gaa atg ctt gtg ggg ttt ccg ccc ttt tat tca gat gac cca 1508
 Met Tyr Glu Met Leu Val Gly Phe Pro Pro Phe Tyr Ser Asp Asp Pro
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 Met Thr Cys Arg Lys
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 tatgcag ata gta aat tgg aga aat tac ttg aaa ttc cca gat gag gtt 1725
 Ile Val Asn Trp Arg Asn Tyr Leu Lys Phe Pro Asp Glu Val
 295 300 305
 aga cta tca cca gaa gcc aag gat ctt att tgt agg ctt tta tgc aat 1773
 Arg Leu Ser Pro Glu Ala Lys Asp Leu Ile Cys Arg Leu Leu Cys Asn
 310 315 320
 gtt gaa caa agg ctt gga aca aaa gga gca gat gaa att aag 1815
 Val Glu Gln Arg Leu Gly Thr Lys Gly Ala Asp Glu Ile Lys
 325 330 335
 gtgttgtatg cgttgttcaa ctttgagatt caaagttccc ttatgttata tcattgtgtg 1875

caattcttaa aaacgatttg actggtttct ttcag ggt cac cct tgg ttt aga Gly His Pro Trp Phe Arg 340	1928
ggc aca gaa tgg gga aaa ttg tat caa atg aaa gct gcc ttt att ccc Gly Thr Glu Trp Gly Lys Leu Tyr Gln Met Lys Ala Ala Phe Ile Pro 345 350 355 360	1976
caa gtt aat gat gag ttg gac acc caa aat ttt gag aaa ttt gaa gag Gln Val Asn Asp Glu Leu Asp Thr Gln Asn Phe Glu Lys Phe Glu Glu 365 370 375	2024
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aag caa gtt cca aag tca gcc aag tca ggt cca tgg aga aag Lys Gln Val Pro Lys Ser Ala Lys Ser Gly Pro Trp Arg Lys 380 385 390	2243
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tac aag aac gta gaa atc gta aat gat gac caa ata cca ggg ata g Tyr Lys Asn Val Glu Ile Val Asn Asp Asp Gln Ile Pro Gly Ile A 410 415 420	2818
gtaattcact taacccccc tccgttgctg aggaagaagc aacaatacta gattaccttg 2878 tgattatcat cgcatgtttg ctgcatttgt aatttgtttt attgtgcag ct gag ttg 2935 la Glu Leu G	
aag aag aag agc aat aag cca aaa agg ccg tct att aaa tct ctc ttt g 2984 Lys Lys Lys Ser Asn Lys Pro Lys Arg Pro Ser Ile Lys Ser Leu Phe G 425 430 435 440	

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 lu Asp Glu Thr Ser Gly Gly
 A 445

 aca aca acc cac caa gga agc ttt ttg aat cta cta ccg acg cag att 3146
 Thr Thr His Gln Gly Ser Phe Leu Asn Leu Leu Pro Thr Gln Ile
 450 455 460

 gaa gat cca gag aaa gaa ggt agt aag tcg agc tca tcc ggg tga 3191
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 35 40 45

Ile Gly Lys Gly Ala Phe Gly Glu Val Arg Ile Cys Arg Glu Lys Gly
 50 55 60

Thr Gly Asn Val Tyr Ala Met Lys Lys Leu Lys Lys Ser Glu Met Leu
 65 70 75 80

Arg Arg Gly Gln Val Val Glu His Val Lys Ala Glu Arg Asn Leu Leu
 85 90 95

Ala Glu Val Asp Ser Asn Cys Ile Val Lys Leu Tyr Cys Ser Phe Gln
 100 105 110

Asp Glu Glu Tyr Leu Tyr Leu Ile Met Glu Tyr Leu Pro Gly Gly Asp
 115 120 125

Met Met Thr Leu Leu Met Arg Lys Asp Thr Leu Thr Glu Asp Glu Ala
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Arg Phe Tyr Ile Gly Glu Thr Val Leu Ala Ile Glu Ser Ile His Lys
 145 150 155 160

His Asn Tyr Ile His Arg Asp Ile Lys Pro Asp Asn Leu Leu Asp
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Lys Asp Gly His Met Lys Leu Ser Asp Phe Gly Leu Cys Lys Pro Leu

180	185	190
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Ser Gly Ala Leu Gln Ser Asp Gly Arg Pro Val Ala Thr Arg Arg Thr		
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Gln Gln Glu Gln Leu Leu Asn Trp Gln Arg Asn Arg Arg Met Leu Ala		
225	230	235
Tyr Ser Thr Val Gly Thr Pro Asp Tyr Ile Ala Pro Glu Val Leu Leu		
245	250	255
Lys Lys Gly Tyr Gly Met Glu Cys Asp Trp Trp Ser Leu Gly Ala Ile		
260	265	270
Met Tyr Glu Met Leu Val Gly Phe Pro Pro Phe Tyr Ser Asp Asp Pro		
275	280	285
Met Thr Thr Cys Arg Lys Ile Val Asn Trp Arg Asn Tyr Leu Lys Phe		
290	295	300
Pro Asp Glu Val Arg Leu Ser Pro Glu Ala Lys Asp Leu Ile Cys Arg		
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Leu Leu Cys Asn Val Glu Gln Arg Leu Gly Thr Lys Gly Ala Asp Glu		
325	330	335
Ile Lys Gly His Pro Trp Phe Arg Gly Thr Glu Trp Gly Lys Leu Tyr		
340	345	350
Gln Met Lys Ala Ala Phe Ile Pro Gln Val Asn Asp Glu Leu Asp Thr		
355	360	365
Gln Asn Phe Glu Lys Phe Glu Glu Thr Asp Lys Gln Val Pro Lys Ser		
370	375	380
Ala Lys Ser Gly Pro Trp Arg Lys Met Leu Ser Ser Lys Asp Ile Asn		
385	390	395
Phe Val Gly Tyr Thr Tyr Lys Asn Val Glu Ile Val Asn Asp Asp Gln		
405	410	415
Ile Pro Gly Ile Ala Glu Leu Lys Lys Ser Asn Lys Pro Lys Arg		
420	425	430
Pro Ser Ile Lys Ser Leu Phe Glu Asp Glu Thr Ser Gly Gly Thr Thr		
435	440	445
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 Met Asn Gly Asp Glu Cys Ala Asn Val Ala Thr Cys Trp Val Thr Ser
 10 15 20 25

cta gct tgt gta gtt gac gcc gga cga tat acg aaa aag gta tcc cac 150
 Leu Ala Cys Val Val Asp Ala Gly Arg Tyr Thr Lys Lys Val Ser His
 30 35 40

gac cgg cga acg agg tgg ccc gcc tgg aaa gca cga cgg gat cgt cat 198
 Asp Arg Arg Thr Arg Trp Pro Ala Trp Lys Ala Arg Arg Asp Arg His
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agt gtc cga agt gat agc ggc cta gac agt cat gca ctt gaa ggt gga 246
 Ser Val Arg Ser Asp Ser Gly Leu Asp Ser His Ala Leu Glu Gly Gly
 60 65 70

aaa cga cgt gag tca tgc gta tca cta gct cac gaa cga gat tat gca 294
 Lys Arg Arg Glu Ser Cys Val Ser Leu Ala His Glu Arg Asp Tyr Ala
 75 80 85

cta acg gca cgg tgg gat cgt agc att gca atg acg gat gac acg aac 342
 Leu Thr Ala Arg Trp Asp Arg Ser Ile Ala Met Thr Asp Asp Thr Asn
 90 95 100 105

cca caa acc caa cgt aaa ttt gag aaa cat act cgg gat gta gaa gct 390
 Pro Gln Thr Gln Arg Lys Phe Glu Lys His Thr Arg Asp Val Glu Ala
 110 115 120

gtt cga ttt tct cca cga gat cgt cta att gta tct gcg ggt gca gat 438
 Val Arg Phe Ser Pro Arg Asp Arg Leu Ile Val Ser Ala Gly Ala Asp
 125 130 135

ggg gta att gca gta tgt ccg gtt gct ggt gaa tgt gat gat gac gat 486
 Gly Val Ile Ala Val Cys Pro Val Ala Gly Glu Cys Asp Asp Asp Asp
 140 145 150

gcc cgt gat ggt cat gaa gat tgt gtt agt agt att tgc ttt tca cca 534
 Ala Arg Asp Gly His Glu Asp Cys Val Ser Ser Ile Cys Phe Ser Pro
 155 160 165

tca cta gaa cac ccg atc ctc ttt tct ggt agt tgt atc tac ttt att 582
 Ser Leu Glu His Pro Ile Leu Phe Ser Gly Ser Cys Ile Tyr Phe Ile

170	175	180	185	
aaa gtg tgg aat gtc aat gga aag aaa tgt agg acg ccg cta aaa aag Lys Val Trp Asn Val Asn Gly Lys Lys Cys Arg Thr Pro Leu Lys Lys 190 195 200				630
cat agt aat ccc gta tct aca cgg aca cag tca gaa gag gga agg cta His Ser Asn Pro Val Ser Thr Arg Thr Gln Ser Glu Glu Gly Arg Leu 205 210 215				678
tgt gca aaa ggt ggt aaa agc ggt gca cgg cta cta ccc gat cta agt Cys Ala Lys Gly Gly Lys Ser Gly Ala Arg Leu Leu Pro Asp Leu Ser 220 225 230				726
act cag gaa caa cta ccc aaa att aat caa gaa aac cct att aat caa Thr Gln Glu Gln Leu Pro Lys Ile Asn Gln Glu Asn Pro Ile Asn Gln 235 240 245				774
att gct ttt tca cct agt ccg ttc gtc gtc acg tgc caa acg gaa aga Ile Ala Phe Ser Pro Ser Pro Phe Val Val Thr Cys Gln Thr Glu Arg 250 255 260 265				822
tcc cta tct caa acg tgg tga ccgtgcaccc gcacggtaa aaagtgcacc Ser Leu Ser Gln Thr Trp 270				873
ggatcgaccc accgaaagcc tgctcgctgg aaaaaaaaaaag agcttttag gccttcgct tttttgaag aaaaaaggct cgcgaaaaaa aaaaagctcg aaatca				979
<210> 72				
<211> 271				
<212> PRT				
<213> Arabidopsis thaliana				
<400> 72				
Met Ile Cys Arg Ile Arg Leu Gly Ser Met Asn Gly Asp Glu Cys Ala 1 5 10 15				
Asn Val Ala Thr Cys Trp Val Thr Ser Leu Ala Cys Val Val Asp Ala 20 25 30				
Gly Arg Tyr Thr Lys Lys Val Ser His Asp Arg Arg Thr Arg Trp Pro 35 40 45				
Ala Trp Lys Ala Arg Arg Asp Arg His Ser Val Arg Ser Asp Ser Gly 50 55 60				
Leu Asp Ser His Ala Leu Glu Gly Gly Lys Arg Arg Glu Ser Cys Val 65 70 75 80				
Ser Leu Ala His Glu Arg Asp Tyr Ala Leu Thr Ala Arg Trp Asp Arg 85 90 95				
Ser Ile Ala Met Thr Asp Asp Thr Asn Pro Gln Thr Gln Arg Lys Phe 100 105 110				

Glu Lys His Thr Arg Asp Val Glu Ala Val Arg Phe Ser Pro Arg Asp
 115 120 125
 Arg Leu Ile Val Ser Ala Gly Ala Asp Gly Val Ile Ala Val Cys Pro
 130 135 140
 Val Ala Gly Glu Cys Asp Asp Asp Ala Arg Asp Gly His Glu Asp
 145 150 155 160
 Cys Val Ser Ser Ile Cys Phe Ser Pro Ser Leu Glu His Pro Ile Leu
 165 170 175
 Phe Ser Gly Ser Cys Ile Tyr Phe Ile Lys Val Trp Asn Val Asn Gly
 180 185 190
 Lys Lys Cys Arg Thr Pro Leu Lys Lys His Ser Asn Pro Val Ser Thr
 195 200 205
 Arg Thr Gln Ser Glu Glu Gly Arg Leu Cys Ala Lys Gly Lys Ser
 210 215 220
 Gly Ala Arg Leu Leu Pro Asp Leu Ser Thr Gln Glu Gln Leu Pro Lys
 225 230 235 240
 Ile Asn Gln Glu Asn Pro Ile Asn Gln Ile Ala Phe Ser Pro Ser Pro
 245 250 255
 Phe Val Val Thr Cys Gln Thr Glu Arg Ser Leu Ser Gln Thr Trp
 260 265 270

<210> 73
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 <212> DNA
 <213> Arabidopsis thaliana

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 <222> (254)..(660)

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 <222> (750)..(1193)

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 taaagaaaaaa gctggagtag aactattta aagtgtcatc atg aag aga cta agc 115
 Met Lys Arg Leu Ser
 1 5

agc tca gat tca atg tgt ggt cta atc tcc act tct aca g gttcttatta 165
 Ser Ser Asp Ser Met Cys Gly Leu Ile Ser Thr Ser Thr A
 10 15

ccatctttgt tctttctact ttttgctaat gtcagacaaa acccatgtga tcctttcttc 225
 actttccact gtttcttta ttgacaag at tca ttt ggt tac aca aca gat gaa 279
 sp Ser Phe Gly Tyr Thr Thr Asp Glu
 20 25

cag agt cca aga ggg tac gga agt aat tac caa tct atg ctt gaa ggt 327
 Gln Ser Pro Arg Gly Tyr Gly Ser Asn Tyr Gln Ser Met Leu Glu Gly
 30 35 40

tac gat gaa gat gct aca cta atc gag gaa tat tcc ggc aac cac cac 375
 Tyr Asp Glu Asp Ala Thr Leu Glu Glu Tyr Ser Gly Asn His His
 45 50 55

cac atg ggt cta tcg gag aag aag aga tta aaa gtt gac caa gtc 423
 His Met Gly Leu Ser Glu Lys Lys Arg Arg Leu Lys Val Asp Gln Val
 60 65 70 75

aaa gct ctt gag aag aat ttc gaa ctt gag aat aaa ctc gaa cct gag 471
 Lys Ala Leu Glu Lys Asn Phe Glu Leu Glu Asn Lys Leu Glu Pro Glu
 80 85 90

agg aaa act aaa tta gca caa gag ctt gga ctt caa cct cgt caa gta 519
 Arg Lys Thr Lys Leu Ala Gln Glu Leu Gly Leu Gln Pro Arg Gln Val
 95 100 105

gct gtt tgg ttt cag aac cgt cgt gca cgg tgg aaa aca aaa cag ctt 567
 Ala Val Trp Phe Gln Asn Arg Arg Ala Arg Trp Lys Thr Lys Gln Leu
 110 115 120

gaa aaa gat tac ggt gtt ctt aag ggt caa tac gat tct ctc cgc cac 615
 Glu Lys Asp Tyr Gly Val Leu Lys Gly Gln Tyr Asp Ser Leu Arg His
 125 130 135

aat ttc gat tct ctc cgc cgt gac aat gat tcc ctt ctc caa gag 660
 Asn Phe Asp Ser Leu Arg Arg Asp Asn Asp Ser Leu Leu Gln Glu
 140 145 150

gtacaatatt agagacttta aaccataaaa attgaaactt cagagacgaa aatgcaaaaa 720
 ggtttgattt tttaaagtttt tggttgcaag att agt aaa atc aaa gct aag gta 773
 Ile Ser Lys Ile Lys Val
 155 160

aac ggt gaa gaa gat aac aac aac aac aaa gct att acg gag ggt gtt 821
 Asn Gly Glu Glu Asp Asn Asn Asn Lys Ala Ile Thr Glu Gly Val
 165 170 175

aag gaa gag gaa gtt cac aag acg gat tcg att cct tcg tct cct ctg 869
 Lys Glu Glu Glu Val His Lys Thr Asp Ser Ile Pro Ser Ser Pro Leu
 180 185 190

cag ttt cta gaa cat tcc tct ggt ttt aac tac cgg cga agc ttc act 917

Gln Phe Leu Glu His Ser Ser Gly Phe Asn Tyr Arg Arg Ser Phe Thr			
195	200	205	210
gac ctc cgt gac ctt cta ccg aat tcc acc gtt gtc gag gct gga tct			965
Asp Leu Arg Asp Leu Leu Pro Asn Ser Thr Val Val Glu Ala Gly Ser			
215	220	225	
tcc gat agt tgc gat tca agc gcc gtt ctt aac gac gaa aca agt tct			1013
Ser Asp Ser Cys Asp Ser Ser Ala Val Leu Asn Asp Glu Thr Ser Ser			
230	235	240	
gat aac gga aga ttg acg ccg cct gtg acg gtt act ggc ggg agt ttc			1061
Asp Asn Gly Arg Leu Thr Pro Pro Val Thr Val Thr Gly Gly Ser Phe			
245	250	255	
tta cag ttt gtg aaa aca gag caa aca gag gat cac gag gat ttt cta			1109
Leu Gln Phe Val Lys Thr Glu Gln Thr Glu Asp His Glu Asp Phe Leu			
260	265	270	
agc ggt gaa gaa gct tgt ggt ttc ttc tcc gat gaa cag ccg ccg tca			1157
Ser Gly Glu Glu Ala Cys Gly Phe Phe Ser Asp Glu Gln Pro Pro Ser			
275	280	285	290
ctt cat tgg tac tct gct tca gat cat tgg act tga gaattgttta			1203
Leu His Trp Tyr Ser Ala Ser Asp His Trp Thr			
295	300		
tcaaatttgtt gctctgttta gtctcaatgg gaaaacagag aagagggcaa aggtgga			1260
<210> 74			
<211> 301			
<212> PRT			
<213> Arabidopsis thaliana			
<400> 74			
Met Lys Arg Leu Ser Ser Ser Asp Ser Met Cys Gly Leu Ile Ser Thr			
1	5	10	15
Ser Thr Asp Ser Phe Gly Tyr Thr Thr Asp Glu Gln Ser Pro Arg Gly			
20	25	30	
Tyr Gly Ser Asn Tyr Gln Ser Met Leu Glu Gly Tyr Asp Glu Asp Ala			
35	40	45	
Thr Leu Ile Glu Glu Tyr Ser Gly Asn His His His Met Gly Leu Ser			
50	55	60	
Glu Lys Lys Arg Arg Leu Lys Val Asp Gln Val Lys Ala Leu Glu Lys			
65	70	75	80
Asn Phe Glu Leu Glu Asn Lys Leu Glu Pro Glu Arg Lys Thr Lys Leu			
85	90	95	
Ala Gln Glu Leu Gly Leu Gln Pro Arg Gln Val Ala Val Trp Phe Gln			
100	105	110	

Asn Arg Arg Ala Arg Trp Lys Thr Lys Gln Leu Glu Lys Asp Tyr Gly
 115 120 125
 Val Leu Lys Gly Gln Tyr Asp Ser Leu Arg His Asn Phe Asp Ser Leu
 130 135 140
 Arg Arg Asp Asn Asp Ser Leu Leu Gln Glu Ile Ser Lys Ile Lys Ala
 145 150 155 160
 Lys Val Asn Gly Glu Glu Asp Asn Asn Asn Lys Ala Ile Thr Glu
 165 170 175
 Gly Val Lys Glu Glu Val His Lys Thr Asp Ser Ile Pro Ser Ser
 180 185 190
 Pro Leu Gln Phe Leu Glu His Ser Ser Gly Phe Asn Tyr Arg Arg Ser
 195 200 205
 Phe Thr Asp Leu Arg Asp Leu Leu Pro Asn Ser Thr Val Val Glu Ala
 210 215 220
 Gly Ser Ser Asp Ser Cys Asp Ser Ser Ala Val Leu Asn Asp Glu Thr
 225 230 235 240
 Ser Ser Asp Asn Gly Arg Leu Thr Pro Pro Val Thr Val Thr Gly Gly
 245 250 255
 Ser Phe Leu Gln Phe Val Lys Thr Glu Gln Thr Glu Asp His Glu Asp
 260 265 270
 Phe Leu Ser Gly Glu Glu Ala Cys Gly Phe Phe Ser Asp Glu Gln Pro
 275 280 285
 Pro Ser Leu His Trp Tyr Ser Ala Ser Asp His Trp Thr
 290 295 300

<210> 75
 <211> 1122
 <212> DNA
 <213> Arabidopsis thaliana

<220>
 <221> CDS
 <222> (22)..(1122)

<400> 75
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 Met Asn Gln Arg Ala Asp Arg Asp Arg Ala
 1 5 10
 agc tcg atc cgt tgg ttt gcc aac cga tta gtg agt ggt agc ctg tta 99
 Ser Ser Ile Arg Trp Phe Ala Asn Arg Leu Val Ser Gly Ser Leu Leu
 15 20 25
 ttg tgt gct aac gcc tac agt cgt cgt act ccc gcg tcc ggg gcc gca 147

Leu Cys Ala Asn Ala Tyr Ser Arg Arg Thr Pro Ala Ser Gly Ala Ala			
30	35	40	
tta cag cag atg aac cgt gcc agt cag tca gtg aat tac cga cga cgt			195
Leu Gln Gln Met Asn Arg Ala Ser Gln Ser Val Asn Tyr Arg Arg Arg			
45	50	55	
gag ctg tca tta atc agc ggc cg ^g aaa cag ggt gtc cag tct ctg ggt			243
Glu Leu Ser Leu Ile Ser Gly Arg Lys Gln Gly Val Gln Ser Leu Gly			
60	65	70	
tat aga ctt gca cgc ctc gat aac cgc gct ctt gca caa ttg ttg cac			291
Tyr Arg Leu Ala Arg Leu Asp Asn Arg Ala Leu Ala Gln Leu Leu His			
75	80	85	90
agg gat ggc cag ccc gag gaa gtg gta cag cgc ggc aat gaa atc agc			339
Arg Asp Gly Gln Pro Glu Glu Val Val Gln Arg Gly Asn Glu Ile Ser			
95	100	105	
tat ttc gaa acg gga ctt gaa ccg acc acg ctt aga cgt gtg cgc gat			387
Tyr Phe Glu Thr Gly Leu Glu Pro Thr Thr Leu Arg Arg Val Arg Asp			
110	115	120	
tgt gtt gtt gcc gct ctg cca acc gtt atc tat acc gga ttc aaa cgt			435
Cys Val Val Ala Ala Leu Pro Thr Val Ile Tyr Thr Gly Phe Lys Arg			
125	130	135	
gtt tct cct tac tac gaa ttt atc tcc gtc ggg cgc acg agg gtt gct			483
Val Ser Pro Tyr Tyr Glu Phe Ile Ser Val Gly Arg Thr Arg Val Ala			
140	145	150	
gat cgt ctt agc gaa gtc acg caa gtg gtt ccc cga gat gat aca cgc			531
Asp Arg Leu Ser Glu Val Thr Gln Val Val Pro Arg Asp Asp Thr Arg			
155	160	165	170
tac gtc tac atc gtg tgg cgg gaa tcc gaa cga tcg aaa tta gag gcg			579
Tyr Val Tyr Ile Val Trp Arg Glu Ser Glu Arg Ser Lys Leu Glu Ala			
175	180	185	
cgg ggg gat ctc cgt gat cgc gat ggt gaa acg ctg gaa aag ttt cgc			627
Arg Gly Asp Leu Arg Asp Arg Asp Gly Glu Thr Leu Glu Lys Phe Arg			
190	195	200	
gtg att gct ttt aac gtc acg ctg gat atc agc agc agt atg gag ccg			675
Val Ile Ala Phe Asn Val Thr Leu Asp Ile Ser Ser Met Glu Pro			
205	210	215	
ctg gcg aag gga gat ttg ccg ccg ttg ctt gct gtt cct gta ggt gaa			723
Leu Ala Lys Gly Asp Leu Pro Pro Leu Leu Ala Val Pro Val Gly Glu			
220	225	230	
caa gct aga ttc agc ttg acg cca acc tgg ttg cca cag ggt cgt agc			771
Gln Ala Arg Phe Ser Leu Thr Pro Thr Trp Leu Pro Gln Gly Arg Ser			
235	240	245	250
gat gtt tcc agt agt cga cgt ggg cta ccg cgg atg gac aaa gtg cct			819
Asp Val Ser Ser Arg Arg Gly Leu Pro Arg Met Asp Lys Val Pro			

255	260	265	
atc gaa tcc cgt ctc tcg acc gac gga gta ttc agc ttc tcg gta aac Ile Glu Ser Arg Leu Ser Thr Asp Gly Val Phe Ser Phe Ser Val Asn 270	275	280	867
gtt aac ggc gct acg cca tcg agg tgg gat cag atg ttg cgc acc gga Val Asn Gly Ala Thr Pro Ser Arg Trp Asp Gln Met Leu Arg Thr Gly 285	290	295	915
cgc agg ccc gtc agt aga agc gta cgt gat gtc gcc gaa aac acc att Arg Arg Pro Val Ser Arg Ser Val Arg Asp Val Ala Glu Asn Thr Ile 300	305	310	963
ggc ggt gaa ctg ccg ccg cgt agc tgc tcg cga ccc gat ccg ttg acc Gly Gly Glu Leu Pro Pro Arg Ser Cys Ser Arg Pro Asp Pro Leu Thr 315	320	325	1011
gct gac cgc cga cgc tgc gct agc ctg agc ctg ccc agc ctg cca gct Ala Asp Arg Arg Cys Ala Ser Leu Ser Leu Pro Ser Leu Pro Ala 335	340	345	1059
cga cag ccc tcc caa acg gag aaa cgc att gtc gag aat att aag tac Arg Gln Pro Ser Gln Thr Glu Lys Arg Ile Val Glu Asn Ile Lys Tyr 350	355	360	1107
ggg gca gcg cca tga Gly Ala Ala Pro 365			1122
 <210> 76			
<211> 366			
<212> PRT			
<213> <i>Arabidopsis thaliana</i>			
 <400> 76			
Met Asn Gln Arg Ala Asp Arg Asp Arg Ala Ser Ser Ile Arg Trp Phe 1	5	10	15
Ala Asn Arg Leu Val Ser Gly Ser Leu Leu Leu Cys Ala Asn Ala Tyr 20	25	30	
Ser Arg Arg Thr Pro Ala Ser Gly Ala Ala Leu Gln Gln Met Asn Arg 35	40	45	
Ala Ser Gln Ser Val Asn Tyr Arg Arg Arg Glu Leu Ser Leu Ile Ser 50	55	60	
Gly Arg Lys Gln Gly Val Gln Ser Leu Gly Tyr Arg Leu Ala Arg Leu 65	70	75	80
Asp Asn Arg Ala Leu Ala Gln Leu Leu His Arg Asp Gly Gln Pro Glu 85	90	95	
Glu Val Val Gln Arg Gly Asn Glu Ile Ser Tyr Phe Glu Thr Gly Leu 100	105	110	

Glu Pro Thr Thr Leu Arg Arg Val Arg Asp Cys Val Val Ala Ala Leu
 115 120 125

Pro Thr Val Ile Tyr Thr Gly Phe Lys Arg Val Ser Pro Tyr Tyr Glu
 130 135 140

Phe Ile Ser Val Gly Arg Thr Arg Val Ala Asp Arg Leu Ser Glu Val
 145 150 155 160

Thr Gln Val Val Pro Arg Asp Asp Thr Arg Tyr Val Tyr Ile Val Trp
 165 170 175

Arg Glu Ser Glu Arg Ser Lys Leu Glu Ala Arg Gly Asp Leu Arg Asp
 180 185 190

Arg Asp Gly Glu Thr Leu Glu Lys Phe Arg Val Ile Ala Phe Asn Val
 195 200 205

Thr Leu Asp Ile Ser Ser Met Glu Pro Leu Ala Lys Gly Asp Leu
 210 215 220

Pro Pro Leu Leu Ala Val Pro Val Gly Glu Gln Ala Arg Phe Ser Leu
 225 230 235 240

Thr Pro Thr Trp Leu Pro Gln Gly Arg Ser Asp Val Ser Ser Arg
 245 250 255

Arg Gly Leu Pro Arg Met Asp Lys Val Pro Ile Glu Ser Arg Leu Ser
 260 265 270

Thr Asp Gly Val Phe Ser Phe Ser Val Asn Val Asn Gly Ala Thr Pro
 275 280 285

Ser Arg Trp Asp Gln Met Leu Arg Thr Gly Arg Arg Pro Val Ser Arg
 290 295 300

Ser Val Arg Asp Val Ala Glu Asn Thr Ile Gly Gly Glu Leu Pro Pro
 305 310 315 320

Arg Ser Cys Ser Arg Pro Asp Pro Leu Thr Ala Asp Arg Arg Arg Cys
 325 330 335

Ala Ser Leu Ser Leu Pro Ser Leu Pro Ala Arg Gln Pro Ser Gln Thr
 340 345 350

Glu Lys Arg Ile Val Glu Asn Ile Lys Tyr Gly Ala Ala Pro
 355 360 365

<210> 77
 <211> 1650
 <212> DNA
 <213> Arabidopsis thaliana
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 Ala Arg Lys Glu Leu Met Ile His Asn Asp Pro Glu Arg Cys Ser Arg
 310 315 320

gag ctt gtg agg gag gcc ctt aaa cg^g aat aca tgt gac aat ttg aca 1476
 Glu Leu Val Arg Glu Ala Leu Lys Arg Asn Thr Cys Asp Asn Leu Thr
 325 330 335

gtg att gtt gtg tgc ttc tct ccg gat cct cca cag agg ata gag atc 1524
 Val Ile Val Val Cys Phe Ser Pro Asp Pro Pro Gln Arg Ile Glu Ile
 340 345 350

cga atg cag tca cgg gtg agg cgg agc ata tct gc^g gaa ggg tta aac 1572
 Arg Met Gln Ser Arg Val Arg Arg Ser Ile Ser Ala Glu Gly Leu Asn
 355 360 365 370

cta ctc aaa ggc gtg ctc gat ggc tat ccg tga gc^atgttatg ttgtacgtta 1625
 Leu Leu Lys Gly Val Leu Asp Gly Tyr Pro
 375 380

ctttgtgaga ctattgccaa gttag 1650

<210> 78
 <211> 380
 <212> PRT
 <213> *Arabidopsis thaliana*

<400> 78
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 1 5 10 15

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 20 25 30

Leu Asp Asp Thr Arg Gln Ile Ser Lys Gly Lys Pro Pro Arg His Leu
 35 40 45

Thr Ser Ser Ala Thr Arg Leu Gln Leu Ala Ala Asn Ala Asp Val Asp
 50 55 60

Val Cys Asn Leu Val Met Lys Ser Leu Asp Asp Lys Ser Glu Phe Leu
 65 70 75 80

Pro Val Tyr Arg Ser Gly Ser Cys Ala Glu Gln Gly Ala Lys Gln Phe
 85 90 95

Met Glu Asp Glu His Ile Cys Ile Asp Asp Leu Val Asn His Leu Gly
 100 105 110

Ala Ala Ile Gln Cys Ser Ser Leu Gly Ala Phe Tyr Gly Val Phe Asp
 115 120 125

Gly His Gly Gly Thr Asp Ala Ala His Phe Val Arg Lys Asn Ile Leu
 130 135 140

Arg Phe Ile Val Glu Asp Ser Ser Phe Pro Leu Cys Val Lys Lys Ala
 145 150 155 160
 Ile Lys Ser Ala Phe Leu Lys Ala Asp Tyr Glu Phe Ala Asp Asp Ser
 165 170 175
 Ser Leu Asp Ile Ser Ser Gly Thr Thr Ala Leu Thr Ala Phe Ile Phe
 180 185 190
 Gly Arg Arg Leu Ile Ile Ala Asn Ala Gly Asp Cys Arg Ala Val Leu
 195 200 205
 Gly Arg Arg Gly Arg Ala Ile Glu Leu Ser Lys Asp His Lys Pro Asn
 210 215 220
 Cys Thr Ala Glu Lys Val Arg Ile Glu Lys Leu Gly Gly Val Val Tyr
 225 230 235 240
 Asp Gly Tyr Leu Asn Gly Gln Leu Ser Val Ala Arg Ala Ile Gly Asp
 245 250 255
 Trp His Met Lys Gly Pro Lys Gly Ser Ala Cys Pro Leu Ser Pro Glu
 260 265 270
 Pro Glu Leu Gln Glu Thr Asp Leu Ser Glu Asp Asp Glu Phe Leu Ile
 275 280 285
 Met Gly Cys Asp Gly Leu Trp Asp Val Met Ser Ser Gln Cys Ala Val
 290 295 300
 Thr Ile Ala Arg Lys Glu Leu Met Ile His Asn Asp Pro Glu Arg Cys
 305 310 315 320
 Ser Arg Glu Leu Val Arg Glu Ala Leu Lys Arg Asn Thr Cys Asp Asn
 325 330 335
 Leu Thr Val Ile Val Val Cys Phe Ser Pro Asp Pro Pro Gln Arg Ile
 340 345 350
 Glu Ile Arg Met Gln Ser Arg Val Arg Arg Ser Ile Ser Ala Glu Gly
 355 360 365
 Leu Asn Leu Leu Lys Gly Val Leu Asp Gly Tyr Pro
 370 375 380

<210> 79
 <211> 589
 <212> DNA
 <213> Arabidopsis thaliana

<220>
 <221> CDS
 <222> (18)..(575)

<400> 79

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1 5 10	
gag gtg cca aag gta gca aca gag gaa tca tcg gca gag gtt aca gat	98
Glu Val Pro Lys Val Ala Thr Glu Glu Ser Ser Ala Glu Val Thr Asp	
15 20 25	
cgt gga ttg ttc gat ttc ttg gga aag aag aaa gac gaa aca aaa cca	146
Arg Gly Leu Phe Asp Phe Leu Gly Lys Lys Lys Asp Glu Thr Lys Pro	
30 35 40	
gag gag act ccg atc gct tca gag ttt gag cag aag gtt cat att tca	194
Glu Glu Thr Pro Ile Ala Ser Glu Phe Glu Gln Lys Val His Ile Ser	
45 50 55	
gag ccg gag cca gag gtt aaa cac gaa agt ctt ctt gaa aag ctt cac	242
Glu Pro Glu Pro Glu Val Lys His Glu Ser Leu Leu Glu Lys Leu His	
60 65 70 75	
cga agc gac agt tct tct agc tcc tca agt gag gaa gaa ggt tca gat	290
Arg Ser Asp Ser Ser Ser Ser Ser Glu Glu Glu Gly Ser Asp	
80 85 90	
ggg gag aag agg aag aag aag gag aag aag aag cca act act gaa	338
Gly Glu Lys Arg Lys Lys Lys Glu Lys Lys Lys Pro Thr Thr Glu	
95 100 105	
gtt gag gta aag gag gaa gag aag aaa ggg ttt atg gag aag ttg aaa	386
Val Glu Val Lys Glu Glu Lys Lys Gly Phe Met Glu Lys Leu Lys	
110 115 120	
gag aag ctt cct gga cac aag aaa cct gaa gac ggt tca gcc gtc gct	434
Glu Lys Leu Pro Gly His Lys Lys Pro Glu Asp Gly Ser Ala Val Ala	
125 130 135	
gcg gca ccg gtg gtt gtt cct cct cct gtg gaa gaa gcg cat cca gtg	482
Ala Ala Pro Val Val Val Pro Pro Pro Val Glu Glu Ala His Pro Val	
140 145 150 155	
gag aag aaa ggg att ctt gag aag att aag gag aag ctt cca gga tac	530
Glu Lys Lys Gly Ile Leu Glu Lys Ile Lys Glu Lys Leu Pro Gly Tyr	
160 165 170	
cac cct aag acc acc gta gag gag gag aag aaa gat aaa gaa taa	575
His Pro Lys Thr Thr Val Glu Glu Lys Lys Asp Lys Glu	
175 180 185	
gaagattatc attaa	590
<210> 80	
<211> 185	
<212> PRT	
<213> Arabidopsis thaliana	
<400> 80	

Met Ala Glu Glu Ile Lys Asn Val Pro Glu Gln Glu Val Pro Lys Val
 1 5 10 15
 Ala Thr Glu Glu Ser Ser Ala Glu Val Thr Asp Arg Gly Leu Phe Asp
 20 25 30
 Phe Leu Gly Lys Lys Asp Glu Thr Lys Pro Glu Glu Thr Pro Ile
 35 40 45
 Ala Ser Glu Phe Glu Gln Lys Val His Ile Ser Glu Pro Glu Pro Glu
 50 55 60
 Val Lys His Glu Ser Leu Leu Glu Lys Leu His Arg Ser Asp Ser Ser
 65 70 75 80
 Ser Ser Ser Ser Glu Glu Glu Gly Ser Asp Gly Glu Lys Arg Lys
 85 90 95
 Lys Lys Lys Glu Lys Lys Pro Thr Thr Glu Val Glu Val Lys Glu
 100 105 110
 Glu Glu Lys Gly Phe Met Glu Lys Leu Lys Glu Lys Leu Pro Gly
 115 120 125
 His Lys Lys Pro Glu Asp Gly Ser Ala Val Ala Ala Ala Pro Val Val
 130 135 140
 Val Pro Pro Pro Val Glu Glu Ala His Pro Val Glu Lys Lys Gly Ile
 145 150 155 160
 Leu Glu Lys Ile Lys Glu Lys Leu Pro Gly Tyr His Pro Lys Thr Thr
 165 170 175
 Val Glu Glu Glu Lys Lys Asp Lys Glu
 180 185

<210> 81
 <211> 1376
 <212> DNA
 <213> Arabidopsis thaliana

<220>
 <221> CDS
 <222> (20)..(1366)

<400> 81
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 Met Ala Ser Asp Lys Gln Lys Ala Glu Arg Ala
 1 5 10
 gag gtt gcg gcg agg cta gcg gct gag gac ttg cat gac att aac aaa 100
 Glu Val Ala Ala Arg Leu Ala Ala Glu Asp Leu His Asp Ile Asn Lys
 15 20 25
 tcc ggt ggt gct gat gtc aca atg tat aag gtg acg gag aga aca act 148

Ser	Gly	Gly	Ala	Asp	Val	Thr	Met	Tyr	Lys	Val	Thr	Glu	Arg	Thr	Thr	
30							35					40				
gaa cat cca ccg gag caa gat agg ccc ggt gtg ata ggt tca gtg ttc															196	
Glu	His	Pro	Pro	Glu	Gln	Asp	Arg	Pro	Gly	Val	Ile	Gly	Ser	Val	Phe	
45						50					55					
agg gct gtc caa gga acg tat gag cat gcg aga gac gct gta gtt gga															244	
Arg	Ala	Val	Gln	Gly	Thr	Tyr	Glu	His	Ala	Arg	Asp	Ala	Val	Val	Gly	
60						65				70		75				
aaa acc cac gaa gcg gct gag tct acc aaa gaa gga gct cag ata gct															292	
Lys	Thr	His	Glu	Ala	Ala	Glu	Ser	Thr	Lys	Glu	Gly	Ala	Gln	Ile	Ala	
80						85				90						
tca gag aaa gcg gtt gga gca aag gac gca acc gtc gag aaa gct aag															340	
Ser	Glu	Lys	Ala	Val	Gly	Ala	Lys	Asp	Ala	Thr	Val	Glu	Lys	Ala	Lys	
95						100				105						
gaa acc gct gat tat act gcg gag aag gtg ggt gag tat aaa gac tat															388	
Glu	Thr	Ala	Asp	Tyr	Thr	Ala	Glu	Lys	Val	Gly	Glu	Tyr	Lys	Asp	Tyr	
110						115				120						
acg gtt gat aaa gct aaa gag gct aag gac aca act gca gag aag gcg															436	
Thr	Val	Asp	Lys	Ala	Lys	Glu	Ala	Lys	Asp	Thr	Thr	Ala	Glu	Lys	Ala	
125						130				135						
aag gag act gct aat tat act gcg gat aag gcg gtg gaa gca aag gat															484	
Lys	Glu	Thr	Ala	Asn	Tyr	Thr	Ala	Asp	Lys	Ala	Val	Glu	Ala	Lys	Asp	
140						145				150		155				
aag acg gcg gag aag att ggt gag tac aaa gac tat gcg gtg gat aag															532	
Lys	Thr	Ala	Glu	Lys	Ile	Gly	Glu	Tyr	Lys	Asp	Tyr	Ala	Val	Asp	Lys	
160						165				170						
gca gta gaa gct aaa gat aag aca gcg gag aag gcg aag gag act tcg															580	
Ala	Val	Glu	Ala	Lys	Asp	Lys	Thr	Ala	Glu	Lys	Ala	Lys	Glu	Thr	Ser	
175						180				185						
aat tat acg gcg gat aag gct aaa gag gct aag gac aag acg gct gag															628	
Asn	Tyr	Thr	Ala	Asp	Lys	Ala	Lys	Glu	Ala	Lys	Asp	Lys	Thr	Ala	Glu	
190						195				200						
aag gtt ggt gag tat aag gat tac acg gtg gac aag gcc gtg gaa gct															676	
Lys	Val	Gly	Glu	Tyr	Lys	Asp	Tyr	Thr	Val	Asp	Lys	Ala	Val	Glu	Ala	
205						210				215						
agg gat tac aca gcg gag aag gct att gaa gca aag gat aag aca gct															724	
Arg	Asp	Tyr	Thr	Ala	Glu	Lys	Ala	Ile	Glu	Ala	Lys	Asp	Lys	Thr	Ala	
220						225				230		235				
gag aag act gga gag tat aag gac tat acg gtg gag aag gcg acg gag															772	
Glu	Lys	Thr	Gly	Glu	Tyr	Lys	Asp	Tyr	Thr	Val	Glu	Lys	Ala	Thr	Glu	
240						245				250						
ggg aaa gat gtt acg gtg agt aag cta gga gag ctg aag gat agt gcc															820	
Gly	Lys	Asp	Val	Thr	Val	Ser	Lys	Leu	Gly	Glu	Leu	Lys	Asp	Ser	Ala	

255	260	265	
gtt gag aca gcg aag aga gct atg ggt ttc ttg tcg ggg aag aca gag Val Glu Thr Ala Lys Arg Ala Met Gly Phe Leu Ser Gly Lys Thr Glu 270 275 280			868
gag gcc aaa gga aaa gct gtg gag acc aaa gat act gcc aag gaa aac Glu Ala Lys Gly Lys Ala Val Glu Thr Lys Asp Thr Ala Lys Glu Asn 285 290 295			916
atg gag aaa gct gga gaa gta aca aga caa aag atg gag gaa atg aga Met Glu Lys Ala Gly Glu Val Thr Arg Gln Lys Met Glu Glu Met Arg 300 305 310 315			964
ttg gaa ggt aaa gag ctc aaa gaa gaa gct gga gca aaa gcc caa gag Leu Glu Gly Lys Glu Leu Lys Glu Ala Gly Ala Lys Ala Gln Glu 320 325 330			1012
gca tct caa aag act agg gag agt act gag tcg gga gct caa aaa gcc Ala Ser Gln Lys Thr Arg Glu Ser Thr Glu Ser Gly Ala Gln Lys Ala 335 340 345			1060
gaa gag acc aaa gat tct cct gcc gtg agg gga aat gaa gca aaa ggg Glu Glu Thr Lys Asp Ser Pro Ala Val Arg Gly Asn Glu Ala Lys Gly 350 355 360			1108
act att ttt ggt gca tta ggg aat gta acg gaa gca ata aag agc aaa Thr Ile Phe Gly Ala Leu Gly Asn Val Thr Glu Ala Ile Lys Ser Lys 365 370 375			1156
ctg aca atg cca tca gac att gtg gag gaa aca cgc gcg gca cgt gag Leu Thr Met Pro Ser Asp Ile Val Glu Glu Thr Arg Ala Ala Arg Glu 380 385 390 395			1204
cat gga ggg acg ggt agg act gtg gtt gaa gtc aag gtc gag gat tca His Gly Gly Thr Gly Arg Thr Val Val Glu Val Lys Val Glu Asp Ser 400 405 410			1252
aag ccg ggt aag gtg gcg act tca ctg aag gcg tcg gat caa atg acc Lys Pro Gly Lys Val Ala Thr Ser Leu Lys Ala Ser Asp Gln Met Thr 415 420 425			1300
ggt caa aca ttc aac gac gtt gga cggt atg gat gat gat gat gct cggt aaa Gly Gln Thr Phe Asn Asp Val Gly Arg Met Asp Asp Asp Ala Arg Lys 430 435 440			1348
gat aag gga aag ctg tga gaatactaga Asp Lys Gly Lys Leu 445			1376

<210> 82
<211> 448
<212> PRT
<213> Arabidopsis thaliana

<400> 82

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 1 5 10 15

Leu Ala Ala Glu Asp Leu His Asp Ile Asn Lys Ser Gly Gly Ala Asp
 20 25 30

Val Thr Met Tyr Lys Val Thr Glu Arg Thr Thr Glu His Pro Pro Glu
 35 40 45

Gln Asp Arg Pro Gly Val Ile Gly Ser Val Phe Arg Ala Val Gln Gly
 50 55 60

Thr Tyr Glu His Ala Arg Asp Ala Val Val Gly Lys Thr His Glu Ala
 65 70 75 80

Ala Glu Ser Thr Lys Glu Gly Ala Gln Ile Ala Ser Glu Lys Ala Val
 85 90 95

Gly Ala Lys Asp Ala Thr Val Glu Lys Ala Lys Glu Thr Ala Asp Tyr
 100 105 110

Thr Ala Glu Lys Val Gly Glu Tyr Lys Asp Tyr Thr Val Asp Lys Ala
 115 120 125

Lys Glu Ala Lys Asp Thr Thr Ala Glu Lys Ala Lys Glu Thr Ala Asn
 130 135 140

Tyr Thr Ala Asp Lys Ala Val Glu Ala Lys Asp Lys Thr Ala Glu Lys
 145 150 155 160

Ile Gly Glu Tyr Lys Asp Tyr Ala Val Asp Lys Ala Val Glu Ala Lys
 165 170 175

Asp Lys Thr Ala Glu Lys Ala Lys Glu Thr Ser Asn Tyr Thr Ala Asp
 180 185 190

Lys Ala Lys Glu Ala Lys Asp Lys Thr Ala Glu Lys Val Gly Glu Tyr
 195 200 205

Lys Asp Tyr Thr Val Asp Lys Ala Val Glu Ala Arg Asp Tyr Thr Ala
 210 215 220

Glu Lys Ala Ile Glu Ala Lys Asp Lys Thr Ala Glu Lys Thr Gly Glu
 225 230 235 240

Tyr Lys Asp Tyr Thr Val Glu Lys Ala Thr Glu Gly Lys Asp Val Thr
 245 250 255

Val Ser Lys Leu Gly Glu Leu Lys Asp Ser Ala Val Glu Thr Ala Lys
 260 265 270

Arg Ala Met Gly Phe Leu Ser Gly Lys Thr Glu Glu Ala Lys Gly Lys
 275 280 285

Ala Val Glu Thr Lys Asp Thr Ala Lys Glu Asn Met Glu Lys Ala Gly
 290 295 300

Glu Val Thr Arg Gln Lys Met Glu Glu Met Arg Leu Glu Gly Lys Glu
 305 310 315 320
 Leu Lys Glu Glu Ala Gly Ala Lys Ala Gln Glu Ala Ser Gln Lys Thr
 325 330 335
 Arg Glu Ser Thr Glu Ser Gly Ala Gln Lys Ala Glu Glu Thr Lys Asp
 340 345 350
 Ser Pro Ala Val Arg Gly Asn Glu Ala Lys Gly Thr Ile Phe Gly Ala
 355 360 365
 Leu Gly Asn Val Thr Glu Ala Ile Lys Ser Lys Leu Thr Met Pro Ser
 370 375 380
 Asp Ile Val Glu Glu Thr Arg Ala Ala Arg Glu His Gly Gly Thr Gly
 385 390 395 400
 Arg Thr Val Val Glu Val Lys Val Glu Asp Ser Lys Pro Gly Lys Val
 405 410 415
 Ala Thr Ser Leu Lys Ala Ser Asp Gln Met Thr Gly Gln Thr Phe Asn
 420 425 430
 Asp Val Gly Arg Met Asp Asp Asp Ala Arg Lys Asp Lys Gly Lys Leu
 435 440 445

<210> 83
 <211> 561
 <212> DNA
 <213> Arabidopsis thaliana

<220>
 <221> CDS
 <222> (18)..(548)

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 1 5 10
 atc gta gta gca tta ttc ttc gat tta act caa gcc tat cgt cac act 98
 Ile Val Val Ala Leu Phe Phe Asp Leu Thr Gln Ala Tyr Arg His Thr
 15 20 25
 ccc gct caa ccg cca aaa gca aac gca aac ggt gat gtc aaa ccg caa 146
 Pro Ala Gln Pro Pro Lys Ala Asn Ala Asn Gly Asp Val Lys Pro Gln
 30 35 40
 gaa acg ctc gtg gtt cac aac aag gcc cga gcc atg gtc gga gtc gga 194
 Glu Thr Leu Val Val His Asn Lys Ala Arg Ala Met Val Gly Val Gly
 45 50 55
 cca atg gtg tgg aac gaa act ctt gcg acc tat gca cag agc tac gca 242
 Pro Met Val Trp Asn Glu Thr Leu Ala Thr Tyr Ala Gln Ser Tyr Ala

60	65	70	75	
cat gaa cga gcc aga gac tgt gcc atg aag cat tcc ttg gga cca ttc His Glu Arg Ala Arg Asp Cys Ala Met Lys His Ser Leu Gly Pro Phe 80		85		290
90				
ggc gag aat cta gcc gcg ggt tgg gga acg atg agc ggt ccg gta gca Gly Glu Asn Leu Ala Ala Gly Trp Gly Thr Met Ser Gly Pro Val Ala 95		100		338
105				
act gag tat tgg atg acg gag aag gaa aat tac gat tat gat agt aac Thr Glu Tyr Trp Met Thr Glu Lys Glu Asn Tyr Asp Tyr Asp Ser Asn 110		115		386
120				
acg tgt ggt ggt gat gtg tgt gga cac tac act cag atc gtg tgg Thr Cys Gly Gly Asp Gly Val Cys Gly His Tyr Thr Gln Ile Val Trp 125		130		434
135				
cgt gac tcg gtt cga ctt ggt tgt gcc tcc gtg aga tgt aag aat gat Arg Asp Ser Val Arg Leu Gly Cys Ala Ser Val Arg Cys Lys Asn Asp 140		145		482
150		155		
gag tat att tgg gtg att tgt agc tat gat cct ccg ggg aat tac atc Glu Tyr Ile Trp Val Ile Cys Ser Tyr Asp Pro Pro Gly Asn Tyr Ile 160		165		530
170				
ggt caa cgt cca tat tag tgattggatt tta Gly Gln Arg Pro Tyr 175				561
<210> 84				
<211> 176				
<212> PRT				
<213> Arabidopsis thaliana				
<400> 84				
Met Asn Glu Met Ser Phe Phe Gly Tyr Ser Phe Ile Val Val Ala Leu 1	5	10	15	
Phe Phe Asp Leu Thr Gln Ala Tyr Arg His Thr Pro Ala Gln Pro Pro 20		25	30	
Lys Ala Asn Ala Asn Gly Asp Val Lys Pro Gln Glu Thr Leu Val Val 35		40	45	
His Asn Lys Ala Arg Ala Met Val Gly Val Gly Pro Met Val Trp Asn 50		55	60	
Glu Thr Leu Ala Thr Tyr Ala Gln Ser Tyr Ala His Glu Arg Ala Arg 65		70	75	80
Asp Cys Ala Met Lys His Ser Leu Gly Pro Phe Gly Glu Asn Leu Ala 85		90	95	
Ala Gly Trp Gly Thr Met Ser Gly Pro Val Ala Thr Glu Tyr Trp Met 100		105	110	

Thr Glu Lys Glu Asn Tyr Asp Tyr Asp Ser Asn Thr Cys Gly Gly Asp
 115 120 125

Gly Val Cys Gly His Tyr Thr Gln Ile Val Trp Arg Asp Ser Val Arg
 130 135 140

Leu Gly Cys Ala Ser Val Arg Cys Lys Asn Asp Glu Tyr Ile Trp Val
 145 150 155 160

Ile Cys Ser Tyr Asp Pro Pro Gly Asn Tyr Ile Gly Gln Arg Pro Tyr
 165 170 175

<210> 85

<211> 988

<212> DNA

<213> Arabidopsis thaliana

<220>

<221> CDS

<222> (12)..(977)

<400> 85

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	Met Ala Ala Ser Lys Arg Leu Val Val Ser Cys Leu Phe	
1	5	10

tta gtt ttg ttg ttt gct caa gcc aat tcg caa ggt ttg aaa gta ggt	98	
Leu Val Leu Leu Phe Ala Gln Ala Asn Ser Gln Gly Leu Lys Val Gly		
15	20	25

ttc tac agc aaa aca tgc cca caa ctc gag ggt ata gtt aaa aag gtc	146		
Phe Tyr Ser Lys Thr Cys Pro Gln Leu Glu Gly Ile Val Lys Lys Val			
30	35	40	45

gtg ttc gat gcg atg aac aaa gca cca aca ctt ggt gct cct ttg ctt	194	
Val Phe Asp Ala Met Asn Lys Ala Pro Thr Leu Gly Ala Pro Leu Leu		
50	55	60

aga atg ttc ttc cac gac tgc ttc gtt cg gga tgg gac gga tca gtt	242	
Arg Met Phe Phe His Asp Cys Phe Val Arg Gly Cys Asp Gly Ser Val		
65	70	75

ttg tta gat aaa cca aac aat caa ggt gag aag agt gca gtt cct aac	290	
Leu Leu Asp Lys Pro Asn Asn Gln Gly Glu Lys Ser Ala Val Pro Asn		
80	85	90

cta agt ctt cga ggg ttt ggc atc ata gac gat tcc aag gcg gct cta	338	
Leu Ser Leu Arg Gly Phe Gly Ile Ile Asp Asp Ser Lys Ala Ala Leu		
95	100	105

gaa aaa gtg tgt ccg gga att gtt tct tgc tct gat atc ttg gca ctt	386		
Glu Lys Val Cys Pro Gly Ile Val Ser Cys Ser Asp Ile Leu Ala Leu			
110	115	120	125

gtc gct aga gac gca atg gtc gca ctt gaa gga cca tca tgg gaa gtt	434
Val Ala Arg Asp Ala Met Val Ala Leu Glu Gly Pro Ser Trp Glu Val	
130 135 140	
gaa acg gga aga aga gac ggt agg gtt tct aac atc aac gaa gtc aac	482
Glu Thr Gly Arg Arg Asp Gly Arg Val Ser Asn Ile Asn Glu Val Asn	
145 150 155	
ttg cca tca cct ttt gat aac atc acc aag ctt atc agc gat ttt cgc	530
Leu Pro Ser Pro Phe Asp Asn Ile Thr Lys Leu Ile Ser Asp Phe Arg	
160 165 170	
tca aag ggc ctc aac gag aag gat cta gtc att ctc tcg ggt ggt cac	578
Ser Lys Gly Leu Asn Glu Lys Asp Leu Val Ile Leu Ser Gly Gly His	
175 180 185	
aca att gga atg gga cat tgt cct tta ttg aca aac cgg ctt tac aac	626
Thr Ile Gly Met Gly His Cys Pro Leu Leu Thr Asn Arg Leu Tyr Asn	
190 195 200 205	
ttc acc gga aaa gga gac agc gac cca agt ttg gac tcg gag tac gcc	674
Phe Thr Gly Lys Gly Asp Ser Asp Pro Ser Leu Asp Ser Glu Tyr Ala	
210 215 220	
gct aag ctc agg aag aaa tgc aag ccc acc gat acg acg acg gct cta	722
Ala Lys Leu Arg Lys Lys Cys Lys Pro Thr Asp Thr Thr Ala Leu	
225 230 235	
gag atg gat ccg ggg agt ttc aaa aca ttt gac ttg agc tac ttc acg	770
Glu Met Asp Pro Gly Ser Phe Lys Thr Phe Asp Leu Ser Tyr Phe Thr	
240 245 250	
cta gtg gct aag aga aga gga ctt ttc cag tcg gat gct gct cta ctc	818
Leu Val Ala Lys Arg Arg Gly Leu Phe Gln Ser Asp Ala Ala Leu Leu	
255 260 265	
gac aac tcc aag act agg gct tat gtc ttg caa cag ata aga act cat	866
Asp Asn Ser Lys Thr Arg Ala Tyr Val Leu Gln Gln Ile Arg Thr His	
270 275 280 285	
ggg tca atg ttc ttt aac gac ttt ggt gtc tct atg gtg aaa atg ggt	914
Gly Ser Met Phe Phe Asn Asp Phe Gly Val Ser Met Val Lys Met Gly	
290 295 300	
cgg act gga gtt ctt acg ggt aag gcc ggg gag atc cgt aag acg tgt	962
Arg Thr Gly Val Leu Thr Gly Lys Ala Gly Glu Ile Arg Lys Thr Cys	
305 310 315	
cgg tct gct aat taa gagatataaa aa	989
Arg Ser Ala Asn	
320	

<210> 86
<211> 321
<212> PRT
<213> Arabidopsis thaliana

<400> 86
 Met Ala Ala Ser Lys Arg Leu Val Val Ser Cys Leu Phe Leu Val Leu
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 20 25 30
 Lys Thr Cys Pro Gln Leu Glu Gly Ile Val Lys Lys Val Val Phe Asp
 35 40 45
 Ala Met Asn Lys Ala Pro Thr Leu Gly Ala Pro Leu Leu Arg Met Phe
 50 55 60
 Phe His Asp Cys Phe Val Arg Gly Cys Asp Gly Ser Val Leu Leu Asp
 65 70 75 80
 Lys Pro Asn Asn Gln Gly Glu Lys Ser Ala Val Pro Asn Leu Ser Leu
 85 90 95
 Arg Gly Phe Gly Ile Ile Asp Asp Ser Lys Ala Ala Leu Glu Lys Val
 100 105 110
 Cys Pro Gly Ile Val Ser Cys Ser Asp Ile Leu Ala Leu Val Ala Arg
 115 120 125
 Asp Ala Met Val Ala Leu Glu Gly Pro Ser Trp Glu Val Glu Thr Gly
 130 135 140
 Arg Arg Asp Gly Arg Val Ser Asn Ile Asn Glu Val Asn Leu Pro Ser
 145 150 155 160
 Pro Phe Asp Asn Ile Thr Lys Leu Ile Ser Asp Phe Arg Ser Lys Gly
 165 170 175
 Leu Asn Glu Lys Asp Leu Val Ile Leu Ser Gly Gly His Thr Ile Gly
 180 185 190
 Met Gly His Cys Pro Leu Leu Thr Asn Arg Leu Tyr Asn Phe Thr Gly
 195 200 205
 Lys Gly Asp Ser Asp Pro Ser Leu Asp Ser Glu Tyr Ala Ala Lys Leu
 210 215 220
 Arg Lys Lys Cys Lys Pro Thr Asp Thr Thr Ala Leu Glu Met Asp
 225 230 235 240
 Pro Gly Ser Phe Lys Thr Phe Asp Leu Ser Tyr Phe Thr Leu Val Ala
 245 250 255
 Lys Arg Arg Gly Leu Phe Gln Ser Asp Ala Ala Leu Leu Asp Asn Ser
 260 265 270
 Lys Thr Arg Ala Tyr Val Leu Gln Gln Ile Arg Thr His Gly Ser Met
 275 280 285
 Phe Phe Asn Asp Phe Gly Val Ser Met Val Lys Met Gly Arg Thr Gly

125

290

295

300

Val Leu Thr Gly Lys Ala Gly Glu Ile Arg Lys Thr Cys Arg Ser Ala
 305 310 315 320

Asn

<210> 87
 <211> 650
 <212> DNA
 <213> *Arabidopsis thaliana*

<220>
 <221> CDS
 <222> (8) .. (634)

<400> 87
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 1 5 10

 tcg ttc tcc tcc caa gtt tct caa aga cct aac acc att tcc ttc ccc 97
 Ser Phe Ser Ser Gln Val Ser Gln Arg Pro Asn Thr Ile Ser Phe Pro
 15 20 25 30

 cgc gcg aat tca gta ttc gca tta ccg gcg aaa tcc gca cgc cgc gct 145
 Arg Ala Asn Ser Val Phe Ala Leu Pro Ala Lys Ser Ala Arg Arg Ala
 35 40 45

 tct cta tct atc acc gcc acg gta tct gct cca ccg gag gag gag gag 193
 Ser Leu Ser Ile Thr Ala Thr Val Ser Ala Pro Pro Glu Glu Glu Glu
 50 55 60

 ata gtt gaa ctg aag aaa tac gtc aaa tcg agg ctt ccc gga gga ttt 241
 Ile Val Glu Leu Lys Lys Tyr Val Lys Ser Arg Leu Pro Gly Gly Phe
 65 70 75

 gct gct cag aag att att ggc act gga cga cgt aag tgc gca atc gct 289
 Ala Ala Gln Lys Ile Ile Gly Thr Gly Arg Arg Lys Cys Ala Ile Ala
 80 85 90

 aga gtt gtt ctt cag gaa ggt act ggg aag gtt atc atc aac tat cgt 337
 Arg Val Val Leu Gln Glu Gly Thr Gly Lys Val Ile Ile Asn Tyr Arg
 95 100 110

 gat gcc aag gag tac ctt cag gga aat cca ttg tgg ctt cag tat gtt 385
 Asp Ala Lys Glu Tyr Leu Gln Gly Asn Pro Leu Trp Leu Gln Tyr Val
 115 120 125

 aaa gta cca ttg gtg act tta gga tat gag aat agc tac gac ata ttt 433
 Lys Val Pro Leu Val Thr Leu Gly Tyr Glu Asn Ser Tyr Asp Ile Phe
 130 135 140

 gtg aaa gcc cat gga ggc ggt ctc tca ggt caa gct caa gca att acc 481
 Val Lys Ala His Gly Gly Leu Ser Gly Gln Ala Gln Ala Ile Thr

Lys Lys Glu Gly Leu Leu Thr Arg Asp Ala Arg Val Val Glu Arg Lys
 180 185 190

Lys Ala Gly Leu Lys Lys Ala Arg Lys Ala Pro Gln Phe Ser Lys Arg
 195 200 205

<210> 89

<211> 1223

<212> DNA

<213> *Arabidopsis thaliana*

<220>

<221> CDS

<222> (16)..(1215)

<400> 89

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 Met Gly Ile Ile Glu Arg Ile Lys Glu Ile Glu Ala
 1 5 10

gag atg gct cgg act cag aag aat aaa gct aca gag tat cat ctt ggt 99
 Glu Met Ala Arg Thr Gln Lys Asn Lys Ala Thr Glu Tyr His Leu Gly
 15 20 25

cag ctc aag gca aag att gca aaa ctc agg aca caa ctg ttg gag cct 147
 Gln Leu Lys Ala Lys Ile Ala Lys Leu Arg Thr Gln Leu Leu Glu Pro
 30 35 40

cca aaa ggt gct agt gga ggc ggg gaa ggt ttt gaa gtt acc aag tat 195
 Pro Lys Gly Ala Ser Gly Gly Glu Gly Phe Glu Val Thr Lys Tyr
 45 50 55 60

ggg cat gga cgt gtt gca ctt ata gga ttt cct agt gtc gga aag tcc 243
 Gly His Gly Arg Val Ala Leu Ile Gly Phe Pro Ser Val Gly Lys Ser
 65 70 75

acg ctt ttg act atg tta act gga aca cat tct gaa gca gcc tca tat 291
 Thr Leu Leu Thr Met Leu Thr Gly Thr His Ser Glu Ala Ala Ser Tyr
 80 85 90

gaa ttt aca aca ctt aca tgc atc cct ggt gta att cac tac aac gac 339
 Glu Phe Thr Thr Leu Thr Cys Ile Pro Gly Val Ile His Tyr Asn Asp
 95 100 105

aca aag att cag ctt ctc gat ctt cct ggg att att gaa ggt gct tcg 387
 Thr Lys Ile Gln Leu Leu Asp Leu Pro Gly Ile Ile Glu Gly Ala Ser
 110 115 120

gaa gga aag ggg cga gga agg cag gtt att gct gtt gca aag tct tcc 435
 Glu Gly Lys Gly Arg Gly Arg Gln Val Ile Ala Val Ala Lys Ser Ser
 125 130 135 140

gac ctt gta ttg atg gtt ctt gat gcc tca aaa agc gaa ggc cac agg 483
 Asp Leu Val Leu Met Val Leu Asp Ala Ser Lys Ser Glu Gly His Arg
 145 150 155

caa ata ttg act aag gaa ctt gag gca gtg ggc ttg cga cta aac aaa Gln Ile Leu Thr Lys Glu Leu Glu Ala Val Gly Leu Arg Leu Asn Lys 160	165	170	531
act cct ccg cag ata tac ttt aaa aag aaa aag act ggt gga atc tct Thr Pro Pro Gln Ile Tyr Phe Lys Lys Lys Lys Thr Gly Gly Ile Ser 175	180	185	579
ttc aac act aca gca ccc ttg act cac att gat gag aag ctc tgt tat Phe Asn Thr Thr Ala Pro Leu Thr His Ile Asp Glu Lys Leu Cys Tyr 190	195	200	627
caa atc ctg cat gaa tac aag att cac aat gct gag gtg cta ttt cgt Gln Ile Leu His Glu Tyr Lys Ile His Asn Ala Glu Val Leu Phe Arg 205	210	215	675
220			
gag aat gcc aca gtg gat gac ttt att gat gtc att gaa ggc aac cgc Glu Asn Ala Thr Val Asp Asp Phe Ile Asp Val Ile Glu Gly Asn Arg 225	230	235	723
240	245	250	
aag tat att aag tgt gtt tat gtc tac atc aaa ata gat gtt gtt gga Lys Tyr Ile Lys Cys Val Tyr Val Tyr Ile Lys Ile Asp Val Val Gly 240	245	250	771
255	260	265	
att gat gat gtg gat aga cta tcc cgg cag cca aat tcc att gtt att Ile Asp Asp Val Asp Arg Leu Ser Arg Gln Pro Asn Ser Ile Val Ile 255	260	265	819
270	275	280	
agc tgc aat ctt aag ctt aac tta gac aga cta ctt gct agg atg tgg Ser Cys Asn Leu Lys Leu Asn Leu Asp Arg Leu Leu Ala Arg Met Trp 270	275	280	867
285	290	295	
gac gaa atg ggc ctt gtg aga gtt tac tcg aag ccg caa ggc cag caa Asp Glu Met Gly Leu Val Arg Val Tyr Ser Lys Pro Gln Gly Gln Gln 285	290	295	915
290	295	300	
cca gat ttc gat gag cct ttt gtc ctc tca tct gat cga ggt ggc tgc Pro Asp Phe Asp Glu Pro Phe Val Leu Ser Ser Asp Arg Gly Gly Cys 305	310	315	963
310	315		
aca gtg gaa gac ttc tgt aac cac gtc cac agg act ctg gtg aag gat Thr Val Glu Asp Phe Cys Asn His Val His Arg Thr Leu Val Lys Asp 320	325	330	1011
325	330		
atg aag tat gca ctc gtt tgg ggc aca agc aca agg cac aat cca cag Met Lys Tyr Ala Leu Val Trp Gly Thr Ser Thr Arg His Asn Pro Gln 335	340	345	1059
340	345		
aat tgt ggt ctt tct caa cat ctt gaa gac gaa gat gtt gtt cag atc Asn Cys Gly Leu Ser Gln His Leu Glu Asp Glu Asp Val Val Gln Ile 350	355	360	1107
350	355	360	
gtc aag aaa aag gag aga gac gaa gga gga aga ggc cgg ttc aag tca Val Lys Lys Lys Glu Arg Asp Glu Gly Gly Arg Gly Arg Phe Lys Ser 365	370	375	1155
365	370	375	

17

cac tca aac gcc cct gct aga att gca gac aga gag aaa aaa gct cct	1203		
His Ser Asn Ala Pro Ala Arg Ile Ala Asp Arg Glu Lys Lys Ala Pro			
385	390		
395			
ctt aag caa taa gcttttag	1223		
Leu Lys Gln			
400			
<210> 90			
<211> 399			
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<213> Arabidopsis thaliana			
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Met Gly Ile Ile Glu Arg Ile Lys Glu Ile Glu Ala Glu Met Ala Arg			
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Thr Gln Lys Asn Lys Ala Thr Glu Tyr His Leu Gly Gln Leu Lys Ala			
20	25	30	
Lys Ile Ala Lys Leu Arg Thr Gln Leu Leu Glu Pro Pro Lys Gly Ala			
35	40	45	
Ser Gly Gly Glu Gly Phe Glu Val Thr Lys Tyr Gly His Gly Arg			
50	55	60	
Val Ala Leu Ile Gly Phe Pro Ser Val Gly Lys Ser Thr Leu Leu Thr			
65	70	75	80
Met Leu Thr Gly Thr His Ser Glu Ala Ala Ser Tyr Glu Phe Thr Thr			
85	90	95	
Leu Thr Cys Ile Pro Gly Val Ile His Tyr Asn Asp Thr Lys Ile Gln			
100	105	110	
Leu Leu Asp Leu Pro Gly Ile Ile Glu Gly Ala Ser Glu Gly Lys Gly			
115	120	125	
Arg Gly Arg Gln Val Ile Ala Val Ala Lys Ser Ser Asp Leu Val Leu			
130	135	140	
Met Val Leu Asp Ala Ser Lys Ser Glu Gly His Arg Gln Ile Leu Thr			
145	150	155	160
Lys Glu Leu Glu Ala Val Gly Leu Arg Leu Asn Lys Thr Pro Pro Gln			
165	170	175	
Ile Tyr Phe Lys Lys Lys Thr Gly Gly Ile Ser Phe Asn Thr Thr			
180	185	190	
Ala Pro Leu Thr His Ile Asp Glu Lys Leu Cys Tyr Gln Ile Leu His			
195	200	205	
Glu Tyr Lys Ile His Asn Ala Glu Val Leu Phe Arg Glu Asn Ala Thr			
210	215	220	

Val Asp Asp Phe Ile Asp Val Ile Glu Gly Asn Arg Lys Tyr Ile Lys
 225 230 235 240
 Cys Val Tyr Val Tyr Ile Lys Ile Asp Val Val Gly Ile Asp Asp Val
 245 250 255
 Asp Arg Leu Ser Arg Gln Pro Asn Ser Ile Val Ile Ser Cys Asn Leu
 260 265 270
 Lys Leu Asn Leu Asp Arg Leu Leu Ala Arg Met Trp Asp Glu Met Gly
 275 280 285
 Leu Val Arg Val Tyr Ser Lys Pro Gln Gly Gln Gln Pro Asp Phe Asp
 290 295 300
 Glu Pro Phe Val Leu Ser Ser Asp Arg Gly Gly Cys Thr Val Glu Asp
 305 310 315 320
 Phe Cys Asn His Val His Arg Thr Leu Val Lys Asp Met Lys Tyr Ala
 325 330 335
 Leu Val Trp Gly Thr Ser Thr Arg His Asn Pro Gln Asn Cys Gly Leu
 340 345 350
 Ser Gln His Leu Glu Asp Glu Asp Val Val Gln Ile Val Lys Lys Lys
 355 360 365
 Glu Arg Asp Glu Gly Gly Arg Gly Arg Phe Lys Ser His Ser Asn Ala
 370 375 380
 Pro Ala Arg Ile Ala Asp Arg Glu Lys Lys Ala Pro Leu Lys Gln
 385 390 395

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 1 5 10

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 Val Tyr Gly Ser Phe Gln Glu Pro Ala Val Val Asn Leu Ile Leu Glu
 15 20 25

tgt gct ccg gtc atg gtt tcc gct caa ctc cac ggc tat cac ttg tat 146
 Cys Ala Pro Val Met Val Ser Ala Gln Leu His Gly Tyr His Leu Tyr
 30 35 40 45

aga ctt aaa ggt cgt ttg cat cca tgt att tct cct tcc gac aat gga	194
Arg Leu Lys Gly Arg Leu His Pro Cys Ile Ser Pro Ser Asn Gly	
50	55
	60
tta atc aat ggc aag ata cta act gga tta aca gat tct cag tta gag	242
Leu Ile Asn Gly Lys Ile Leu Thr Gly Leu Thr Asp Ser Gln Leu Glu	
65	70
	75
agt tta gat atg att gaa gga act gaa tat gtg agg aag act gtt gaa	290
Ser Leu Asp Met Ile Glu Gly Thr Glu Tyr Val Arg Lys Thr Val Glu	
80	85
	90
gtt gtt ttg act gat act ttg gag aag aag caa gtt gaa aca att gta	338
Val Val Leu Thr Asp Thr Leu Glu Lys Lys Gln Val Glu Thr Ile Val	
95	100
	105
tgg gca aac aag gat gat cct aat atg tat gga gaa tgg gat ttc gag	386
Trp Ala Asn Lys Asp Asp Pro Asn Met Tyr Gly Glu Trp Asp Phe Glu	
110	115
	120
	125
gaa tgg aag agg ctt cat atg gag aaa ttt ata gag gcg gcg acg aaa	434
Glu Trp Lys Arg Leu His Met Glu Lys Phe Ile Glu Ala Ala Thr Lys	
130	135
	140
ttc atg gag tgg aag aag aat ccg aat ggg aga agt agg gaa gag ttt	482
Phe Met Glu Trp Lys Lys Asn Pro Asn Gly Arg Ser Arg Glu Glu Phe	
145	150
	155
gag aag ttt gta caa gat gat tct tct ccg gct tcg gct tga	524
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	30
Val Met Val Ser Ala Gln Leu His Gly Tyr His Leu Tyr Arg Leu Lys	
35	40
	45
Gly Arg Leu His Pro Cys Ile Ser Pro Ser Asp Asn Gly Leu Ile Asn	
50	55
	60
Gly Lys Ile Leu Thr Gly Leu Thr Asp Ser Gln Leu Glu Ser Leu Asp	
65	70
	75
	80
Met Ile Glu Gly Thr Glu Tyr Val Arg Lys Thr Val Glu Val Val Leu	

85	90	95
Thr Asp Thr Leu Glu Lys Lys Gln Val Glu Thr Ile Val Trp Ala Asn		
100	105	110
Lys Asp Asp Pro Asn Met Tyr Gly Glu Trp Asp Phe Glu Glu Trp Lys		
115	120	125
Arg Leu His Met Glu Lys Phe Ile Glu Ala Ala Thr Lys Phe Met Glu		
130	135	140
Trp Lys Lys Asn Pro Asn Gly Arg Ser Arg Glu Glu Phe Glu Lys Phe		
145	150	155
Val Gln Asp Asp Ser Ser Pro Ala Ser Ala		
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Met Ala Gly Ser Asn Cys Gly Cys Gly Ser Ser Cys		
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aaa tgt ggt gat tcg tgc ag gtaaaccccta gattctctct tcattaactt		101
Lys Cys Gly Asp Ser Cys Se		
15		
atcatgcata tatatcctaa tatacatgtg gttacatatt ccttaagata aattttgaaa	161	
tcttatactt ctgttgtttt ttggatatga caaag t tgc gag aag aac tac aac	215	
r Cys Glu Lys Asn Tyr Asn		
20		25
aag gag tgt gat aac tgt agc tgt gga tca aac tgc agc tgc ggg tca	263	
Lys Glu Cys Asp Asn Cys Ser Cys Gly Ser Asn Cys Ser Cys Gly Ser		
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Ser Cys Asn Cys		
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20 25 30
Cys Gly Ser Asn Cys Ser Cys Gly Ser Ser Cys Asn Cys
35 40 45

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1 5 10
cgc ctc aga tct ctc gct ctt tcg tct ttt tct tct ttc cga ttt 97
Arg Leu Arg Ser Leu Ala Leu Ser Ser Phe Ser Ser Phe Arg Phe
15 20 25
gcc cat cgt cct ctg tca tcg att tca ccg aga aag tta ccg aat ttt 145
Ala His Arg Pro Leu Ser Ser Ile Ser Pro Arg Lys Leu Pro Asn Phe
30 35 40
cgt gct ttc tct ggt acc gct atg aca gat act aaa gat gct ggt atg 193
Arg Ala Phe Ser Gly Thr Ala Met Thr Asp Thr Lys Asp Ala Gly Met
45 50 55 60
gat gct gtt cag aga cgt ctc atg ttt gag gat gaa tgc att ctt gtt 241
Asp Ala Val Gln Arg Arg Leu Met Phe Glu Asp Glu Cys Ile Leu Val
65 70 75
gat gaa act gat cgt gtt gtg ggg cat gac agc aag tat aat tgt cat 289
Asp Glu Thr Asp Arg Val Val Gly His Asp Ser Lys Tyr Asn Cys His
80 85 90
ctg atg gaa aat att gaa gcc aag aat ttg ctg cac agg gct ttt agt 337
Leu Met Glu Asn Ile Glu Ala Lys Asn Leu Leu His Arg Ala Phe Ser
95 100 105
gta ttt tta ttc aac tcg aag tat gag ttg ctt ctc cag caa agg tca 385
Val Phe Leu Phe Asn Ser Lys Tyr Glu Leu Leu Gln Gin Arg Ser
110 115 120

aac aca aag gtt acg ttc cct cta gtg tgg act aac act tgt tgc agc	433
Asn Thr Lys Val Thr Phe Pro Leu Val Trp Thr Asn Thr Cys Cys Ser	
125 130 135 140	
cat cct ctt tac cgt gaa tca gag ctt atc cag gac aat gca cta ggt	481
His Pro Leu Tyr Arg Glu Ser Glu Leu Ile Gln Asp Asn Ala Leu Gly	
145 150 155	
gtg agg aat gct gca caa aga aag ctt ctc gat gag ctt ggt att gta	529
Val Arg Asn Ala Ala Gln Arg Lys Leu Leu Asp Glu Leu Gly Ile Val	
160 165 170	
gct gaa gat gta cca gtc gat gag ttc act ccc ttg gga cgt atg ctg	577
Ala Glu Asp Val Pro Val Asp Glu Phe Thr Pro Leu Gly Arg Met Leu	
175 180 185	
tac aag gct cct tct gat ggc aaa tgg gga gag cat gaa ctt gat tac	625
Tyr Lys Ala Pro Ser Asp Gly Lys Trp Gly Glu His Glu Leu Asp Tyr	
190 195 200	
ttg ctc ttc atc gtg cga gac gtg aag gtt caa cca aac cca gat gaa	673
Leu Leu Phe Ile Val Arg Asp Val Lys Val Gln Pro Asn Pro Asp Glu	
205 210 215 220	
gta gct gag atc aag tat gtg agc cgg gaa gag ctg aag gag ctg gtg	721
Val Ala Glu Ile Lys Tyr Val Ser Arg Glu Glu Leu Lys Glu Leu Val	
225 230 235	
aag aaa gca gat gca ggt gag gaa ggt ttg aaa ctg tca cca tgg ttc	769
Lys Lys Ala Asp Ala Gly Glu Gly Leu Lys Leu Ser Pro Trp Phe	
240 245 250	
aga ttg gtg gtg gac aat ttc ttg atg aag tgg tgg gat cat gta gag	817
Arg Leu Val Val Asp Asn Phe Leu Met Lys Trp Trp Asp His Val Glu	
255 260 265	
aaa gga act ttg gtt gaa gct ata gac atg aaa acc atc cac aaa ctc	865
Lys Gly Thr Leu Val Glu Ala Ile Asp Met Lys Thr Ile His Lys Leu	
270 275 280	
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20 25 30	

Leu Ser Ser Ile Ser Pro Arg Lys Leu Pro Asn Phe Arg Ala Phe Ser
35 40 45

Gly Thr Ala Met Thr Asp Thr Lys Asp Ala Gly Met Asp Ala Val Gln
50 55 60

Arg Arg Leu Met Phe Glu Asp Glu Cys Ile Leu Val Asp Glu Thr Asp
65 70 75 80

Arg Val Val Gly His Asp Ser Lys Tyr Asn Cys His Leu Met Glu Asn
85 90 95

Ile Glu Ala Lys Asn Leu Leu His Arg Ala Phe Ser Val Phe Leu Phe
100 105 110

Asn Ser Lys Tyr Glu Leu Leu Gln Gln Arg Ser Asn Thr Lys Val
115 120 125

Thr Phe Pro Leu Val Trp Thr Asn Thr Cys Cys Ser His Pro Leu Tyr
130 135 140

Arg Glu Ser Glu Leu Ile Gln Asp Asn Ala Leu Gly Val Arg Asn Ala
145 150 155 160

Ala Gln Arg Lys Leu Leu Asp Glu Leu Gly Ile Val Ala Glu Asp Val
165 170 175

Pro Val Asp Glu Phe Thr Pro Leu Gly Arg Met Leu Tyr Lys Ala Pro
180 185 190

Ser Asp Gly Lys Trp Gly Glu His Glu Leu Asp Tyr Leu Leu Phe Ile
195 200 205

Val Arg Asp Val Lys Val Gln Pro Asn Pro Asp Glu Val Ala Glu Ile
210 215 220

Lys Tyr Val Ser Arg Glu Glu Leu Lys Glu Leu Val Lys Lys Ala Asp
225 230 235 240

Ala Gly Glu Glu Gly Leu Lys Leu Ser Pro Trp Phe Arg Leu Val Val
245 250 255

Asp Asn Phe Leu Met Lys Trp Trp Asp His Val Glu Lys Gly Thr Leu
260 265 270

Val Glu Ala Ile Asp Met Lys Thr Ile His Lys Leu
275 280

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1 5 10	
gcc ttc gcc ggt aag gcc gtc aag ctt tcc ccc gcg gca tca gaa gtc	98
Ala Phe Ala Gly Lys Ala Val Lys Leu Ser Pro Ala Ala Ser Glu Val	
15 20 25	
ctt gga agc ggc cgt gtg aca atg agg aag act gtt gcc aag cca aag	146
Leu Gly Ser Gly Arg Val Thr Met Arg Lys Thr Val Ala Lys Pro Lys	
30 35 40	
ggc cca tca ggc agc cca tgg tac gga tct gac cgt gtc aag tac ttg	194
Gly Pro Ser Gly Ser Pro Trp Tyr Gly Ser Asp Arg Val Lys Tyr Leu	
45 50 55	
ggc cca ttc tct ggc gaa tca ccg agc tac ctt acc gga gag ttc ccc	242
Gly Pro Phe Ser Gly Glu Ser Pro Ser Tyr Leu Thr Gly Glu Phe Pro	
60 65 70 75	
gga gac tac gga tgg gac acc gcc gga ctt tca gct gac ccc gag aca	290
Gly Asp Tyr Gly Trp Asp Thr Ala Gly Leu Ser Ala Asp Pro Glu Thr	
80 85 90	
ttc gca agg aac cgt gaa cta gaa gtt atc cac agc agg tgg gct atg	338
Phe Ala Arg Asn Arg Glu Leu Glu Val Ile His Ser Arg Trp Ala Met	
95 100 105	
ctc gga gcc cta ggc tgc gtc ttc cct gag ctt ttg gct aga aac gga	386
Leu Gly Ala Leu Gly Cys Val Phe Pro Glu Leu Leu Ala Arg Asn Gly	
110 115 120	
gtc aag ttc gga gag gcg gtt tgg ttc aag gcc ggt tca cag atc ttc	434
Val Lys Phe Gly Ala Val Trp Phe Lys Ala Gly Ser Gln Ile Phe	
125 130 135	
agc gat gga ggg ctc gat tac ttg gga aac cct agc ttg gtt cac gct	482
Ser Asp Gly Gly Leu Asp Tyr Leu Gly Asn Pro Ser Leu Val His Ala	
140 145 150 155	
cag agc att ttg gcc att tgg gcc aca caa gtt att ttg atg gga gcc	530
Gln Ser Ile Leu Ala Ile Trp Ala Thr Gln Val Ile Leu Met Gly Ala	
160 165 170	
gtt gaa ggc tac aga gtc gca gga aat ggg cca ttg gga gag gcc gag	578
Val Glu Gly Tyr Arg Val Ala Gly Asn Gly Pro Leu Gly Glu Ala Glu	
175 180 185	
gac ttg ctt tac ccc ggt ggc agc ttc gac cca ttg ggt ttg gct acc	626
Asp Leu Leu Tyr Pro Gly Gly Ser Phe Asp Pro Leu Gly Leu Ala Thr	
190 195 200	
gac cca gag gca ttc gct gag ttg aag gtg aag gag ctc aag aac gga	674

Asp Pro Glu Ala Phe Ala Glu Leu Lys Val Lys Glu Leu Lys Asn Gly			
205	210	215	
aga ttg gct atg ttc tct atg ttt gga ttc ttc gtt caa gcc atc gtc		722	
Arg Leu Ala Met Phe Ser Met Phe Gly Phe Phe Val Gln Ala Ile Val			
220	225	230	235
act ggt aag gga ccg ata gag aac ctt gct gac cat ttg gcc gat cca		770	
Thr Gly Lys Gly Pro Ile Glu Asn Leu Ala Asp His Leu Ala Asp Pro			
240	245	250	
gtt aac aac aac gca tgg gcc ttc gcc acc aac ttt gtt ccc gga aag		818	
Val Asn Asn Asn Ala Trp Ala Phe Ala Thr Asn Phe Val Pro Gly Lys			
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Ala Val Lys Leu Ser Pro Ala Ala Ser Glu Val Leu Gly Ser Gly Arg			
20	25	30	
Val Thr Met Arg Lys Thr Val Ala Lys Pro Lys Gly Pro Ser Gly Ser			
35	40	45	
Pro Trp Tyr Gly Ser Asp Arg Val Lys Tyr Leu Gly Pro Phe Ser Gly			
50	55	60	
Glu Ser Pro Ser Tyr Leu Thr Gly Glu Phe Pro Gly Asp Tyr Gly Trp			
65	70	75	80
Asp Thr Ala Gly Leu Ser Ala Asp Pro Glu Thr Phe Ala Arg Asn Arg			
85	90	95	
Glu Leu Glu Val Ile His Ser Arg Trp Ala Met Leu Gly Ala Leu Gly			
100	105	110	
Cys Val Phe Pro Glu Leu Leu Ala Arg Asn Gly Val Lys Phe Gly Glu			
115	120	125	
Ala Val Trp Phe Lys Ala Gly Ser Gln Ile Phe Ser Asp Gly Gly Leu			
130	135	140	
Asp Tyr Leu Gly Asn Pro Ser Leu Val His Ala Gln Ser Ile Leu Ala			
145	150	155	160
Ile Trp Ala Thr Gln Val Ile Leu Met Gly Ala Val Glu Gly Tyr Arg			
165	170	175	

Val Ala Gly Asn Gly Pro Leu Gly Glu Ala Glu Asp Leu Leu Tyr Pro
 180 185 190

 Gly Gly Ser Phe Asp Pro Leu Gly Leu Ala Thr Asp Pro Glu Ala Phe
 195 200 205

 Ala Glu Leu Lys Val Lys Glu Leu Lys Asn Gly Arg Leu Ala Met Phe
 210 215 220

 Ser Met Phe Gly Phe Phe Val Gln Ala Ile Val Thr Gly Lys Gly Pro
 225 230 235 240

 Ile Glu Asn Leu Ala Asp His Leu Ala Asp Pro Val Asn Asn Asn Ala
 245 250 255

 Trp Ala Phe Ala Thr Asn Phe Val Pro Gly Lys
 260 265

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aca gcc act aga aga gtt ctc atc gct ctt cac gag aag aat gtc gac 98
 Thr Ala Thr Arg Arg Val Leu Ile Ala Leu His Glu Lys Asn Val Asp
 15 20 25

ttt gaa ttc gtt cat gtc gag ctc aaa gat ggt gaa cac aag aaa gag 146
 Phe Glu Phe Val His Val Glu Leu Lys Asp Gly Glu His Lys Lys Glu
 30 35 40

cct ttc atc ctt cgc aac gtgagtagat ataacatctg tcaaggccaaa 194
 Pro Phe Ile Leu Arg Asn
 45 50

atattgtatt tcatcttagat actgaatctt ggtcttaaca atcttgaata atgttttgc 254

ag ccc ttt ggt aaa gtt cca gcc ttt gaa gat gga gac ttc aag att 301
 Pro Phe Gly Lys Val Pro Ala Phe Glu Asp Gly Asp Phe Lys Ile
 55 60 65

 ttc g gttaatacaa atatatatca ttatagtcat gtttacaat ttttggtttt 355
 Phe G

 atgatcattt caataataga aaggcggaaac actcaaaaat gttttttttt tggtggcag 415

 aa tca aga gca att act caa tac ata gct cat gaa ttc tca gac aaa 462
 lu Ser Arg Ala Ile Thr Gln Tyr Ile Ala His Glu Phe Ser Asp Lys
 70 75 80

 gga aac aac ctt ctc tca act ggc aag gac atg gcg atc ata gcc atg 510
 Gly Asn Asn Leu Leu Ser Thr Gly Lys Asp Met Ala Ile Ala Met
 85 90 95

 ggc att gaa att gag tcg cat gag ttt gac cca gtt ggt tca aag ctt 558
 Gly Ile Glu Ile Glu Ser His Glu Phe Asp Pro Val Gly Ser Lys Leu
 100 105 110

 gtt tgg gag caa gtc tta aag cct ttg tat ggt atg acc aca gac aaa 606
 Val Trp Glu Gln Val Leu Lys Pro Leu Tyr Gly Met Thr Thr Asp Lys
 115 120 125

 act gtt gtt gaa gaa gaa gag gct aag cta gcc aaa gtc ctc gat gtt 654
 Thr Val Val Glu Glu Glu Ala Lys Leu Ala Lys Val Leu Asp Val
 130 135 140 145

 tac gaa cac agg ctt ggt gag tcc aag tat ttg gct tct gac cac ttc 702
 Tyr Glu His Arg Leu Gly Glu Ser Lys Tyr Leu Ala Ser Asp His Phe
 150 155 160

 act ttg gtc gat ctt cac act atc cct gtg att caa tac tta ctt gga 750
 Thr Leu Val Asp Leu His Thr Ile Pro Val Ile Gln Tyr Leu Leu Gly
 165 170 175

 act cca act aag aaa ctc ttc gac gag cgt cca cat gtg agt gct tgg 798
 Thr Pro Thr Lys Lys Leu Phe Asp Glu Arg Pro His Val Ser Ala Trp
 180 185 190

 gtt gct gac atc act tca agg cct tct gct cag aag gtt ctt taa 843
 Val Ala Asp Ile Thr Ser Arg Pro Ser Ala Gln Lys Val Leu
 195 200 205

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 His Val Glu Leu Lys Asp Gly Glu His Lys Lys Glu Pro Phe Ile Leu
 35 40 45

 Arg Asn Pro Phe Gly Lys Val Pro Ala Phe Glu Asp Gly Asp Phe Lys
 50 55 60

 Ile Phe Glu Ser Arg Ala Ile Thr Gln Tyr Ile Ala His Glu Phe Ser
 65 70 75 80

 Asp Lys Gly Asn Asn Leu Leu Ser Thr Gly Lys Asp Met Ala Ile Ile
 85 90 95

 Ala Met Gly Ile Glu Ile Glu Ser His Glu Phe Asp Pro Val Gly Ser
 100 105 110

 Lys Leu Val Trp Glu Gln Val Leu Lys Pro Leu Tyr Gly Met Thr Thr
 115 120 125

 Asp Lys Thr Val Val Glu Glu Glu Ala Lys Leu Ala Lys Val Leu
 130 135 140

 Asp Val Tyr Glu His Arg Leu Gly Glu Ser Lys Tyr Leu Ala Ser Asp
 145 150 155 160

 His Phe Thr Leu Val Asp Leu His Thr Ile Pro Val Ile Gln Tyr Leu
 165 170 175

 Leu Gly Thr Pro Thr Lys Lys Leu Phe Asp Glu Arg Pro His Val Ser
 180 185 190

 Ala Trp Val Ala Asp Ile Thr Ser Arg Pro Ser Ala Gln Lys Val Leu
 195 200 205

<210> 101
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1	5	10	
acc gct ggc aaa gct ga ggtactactc tttctctctt tgacagaact			97
Thr Ala Gly Lys Ala Gl			15
cttaaactgg aaaaattgtt gaagctataa ctcttgaaa acagttgaaa cttgatcatt			157
actagaaatt tcagttactt gtttaattta gtttgcgtt attatgtat tgatgatttt			217
atggttacaa tgggtgtcat gta g gag aag agc aat gtt ctg ctg gac aag			268
u Glu Lys Ser Asn Val Leu Leu Asp Lys			
20		25	
gcc aag gat gct gca gct ggt gct gga gct gga gca caa ca ggtaaacaat			319
Ala Lys Asp Ala Ala Gly Ala Gly Ala Gly Ala Gln Gl			
30	35	40	
ccatacacag acacataaca tataatatgt aacgaaataa acgtctttgt aagcttacat			379
gtacgcagat ttctgatatg gttatgtata tgttata g gcg gga aag agt gta			432
n Ala Gly Lys Ser Val			
45			
tcg gat gcg gca gcg gga ggt gtt aac ttc gtg aag gac aag acc ggc			480
Ser Asp Ala Ala Gly Gly Val Asn Phe Val Lys Asp Lys Thr Gly			
50	55	60	
ctg aac aag tag agattcgggt caaatttggg			512
Leu Asn Lys			
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Lys Ala Glu Glu Lys Ser Asn Val Leu Leu Asp Lys Ala Lys Asp Ala			
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Ala Ala Gly Ala Gly Ala Gln Gln Ala Gly Lys Ser Val Ser			
35	40	45	
Asp Ala Ala Gly Gly Val Asn Phe Val Lys Asp Lys Thr Gly Leu			
50	55	60	
Asn Lys			
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<210> 103
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<220>
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<400> 103

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	1						5				10			

gaa ggg aag cat tac ttc tca atg tgg caa act ctg ttc gag atc gac

Glu	Gly	Lys	His	Tyr	Phe	Ser	Met	Trp	Gln	Thr	Leu	Phe	Glu	Ile	Asp	97
15							20							25		

act aag tac atg cct atc aag cct att ggt cgt gga gct tac ggt gtt

Thr	Lys	Tyr	Met	Pro	Ile	Lys	Pro	Ile	Gly	Arg	Gly	Ala	Tyr	Gly	Val	145
30							35					40		45		

gtc tgc tcc tct gtt aac agt gac acc aac gag aaa gtt gct atc aag

Val	Cys	Ser	Ser	Val	Asn	Ser	Asp	Thr	Asn	Glu	Lys	Val	Ala	Ile	Lys	193
							50				55		60			

aag att cac aat gtt tat gag aat agg atc gat gcg ttg agg act ctt

Lys	Ile	His	Asn	Val	Tyr	Glu	Asn	Arg	Ile	Asp	Ala	Leu	Arg	Thr	Leu	241
							65				70		75			

cg^g gag ctc aag ctt cta cgc cat ctt cga cat gag aat gtc att gct

Arg	Glu	Leu	Lys	Leu	Leu	Arg	His	Leu	Arg	His	Glu	Asn	Val	Ile	Ala	289
							80				85		90			

ttg aaa gat gtc atg atg cca att cat aag atg agc ttc aag gat gtt

Leu	Lys	Asp	Val	Met	Met	Pro	Ile	His	Lys	Met	Ser	Phe	Lys	Asp	Val	337
							95				100		105			

tat ctt gtt tat gag ctc atg gac act gat ctc cac cag att atc aag

Tyr	Leu	Val	Tyr	Glu	Leu	Met	Asp	Thr	Asp	Leu	His	Gln	Ile	Ile	Lys	385
110							115				120		125			

tct tct cag cgt ctt agt aac gat cat tgc caa tac ttc ttg ttc cag

Ser	Ser	Gln	Arg	Leu	Ser	Asn	Asp	His	Cys	Gln	Tyr	Phe	Leu	Phe	Gln	433
							130				135		140			

ttg ctt cga ggg ctc aag tat att cat tca gcc aat atc ctg cac cga

Leu	Leu	Arg	Gly	Leu	Lys	Tyr	Ile	His	Ser	Ala	Asn	Ile	Leu	His	Arg	481
							145				150		155			

gat ttg aaa cct ggt aac ctt ctt gtc aac gca aac tgc gat tta aag

Asp	Leu	Lys	Pro	Gly	Asn	Leu	Leu	Val	Asn	Ala	Asn	Cys	Asp	Leu	Lys	529
							160				165		170			

ata tgc gat ttt gga cta gcg cgt gcg agc aac acc aag ggt cag ttc

Ile	Cys	Asp	Phe	Gly	Leu	Ala	Arg	Ala	Ser	Asn	Thr	Lys	Gly	Gln	Phe	577
							175				180		185			

atg act gaa tat gtt gtg act cgt tgg tac cga gcc cca gag ctt ctc	625
Met Thr Glu Tyr Val Val Thr Arg Trp Tyr Arg Ala Pro Glu Leu Leu	
190 195 200 205	
ctc tgt tgt gac aac tat gga aca tcc att gat gtt tgg tct gtt ggt	673
Leu Cys Cys Asp Asn Tyr Gly Thr Ser Ile Asp Val Trp Ser Val Gly	
210 215 220	
tgc att ttc gcc gag ctt ctt ggt agg aaa ccg ata ttc caa gga acg	721
Cys Ile Phe Ala Glu Leu Leu Gly Arg Lys Pro Ile Phe Gln Gly Thr	
225 230 235	
gaa tgt ctt aac cag ctt aag ctc att gtc aac att atc gga agc caa	769
Glu Cys Leu Asn Gln Leu Lys Leu Ile Val Asn Ile Ile Gly Ser Gln	
240 245 250	
aga gaa gaa gat ctt gag ttc ata gtt aac ccg aaa gct aaa aga tac	817
Arg Glu Glu Asp Leu Glu Phe Ile Val Asn Pro Lys Ala Lys Arg Tyr	
255 260 265	
att aga tca ctt ccg tac tca cct ggg atg tct tta tcc aga ctt tac	865
Ile Arg Ser Leu Pro Tyr Ser Pro Gly Met Ser Leu Ser Arg Leu Tyr	
270 275 280 285	
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Pro Cys Ala His Val Leu Ala Ile Asp Leu Leu Gln Lys Met Leu Val	
290 295 300	
ttt gat ccg tca aag agg att agt gcc tct gaa gca ctc cag cat cca	961
Phe Asp Pro Ser Lys Arg Ile Ser Ala Ser Glu Ala Leu Gln His Pro	
305 310 315	
tac atg gcg cca cta tat gac ccg aat gca aac cct cct gct caa gtt	1009
Tyr Met Ala Pro Leu Tyr Asp Pro Asn Ala Asn Pro Pro Ala Gln Val	
320 325 330	
cct atc gat ctc gat gta gat gag gat ttg aga gag gag atg ata aga	1057
Pro Ile Asp Leu Asp Val Asp Glu Asp Leu Arg Glu Glu Met Ile Arg	
335 340 345	
gaa atg ata tgg aat gag atg ctt cac tac cat cca caa gct tca acc	1105
Glu Met Ile Trp Asn Glu Met Leu His Tyr His Pro Gln Ala Ser Thr	
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				35				40						45	
Ser	Val	Asn	Ser	Asp	Thr	Asn	Glu	Lys	Val	Ala	Ile	Lys	Lys	Ile	His
				50				55				60			
Asn	Val	Tyr	Glu	Asn	Arg	Ile	Asp	Ala	Leu	Arg	Thr	Leu	Arg	Glu	Leu
				65			70			75			80		
Lys	Leu	Leu	Arg	His	Leu	Arg	His	Glu	Asn	Val	Ile	Ala	Leu	Lys	Asp
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Val	Met	Met	Pro	Ile	His	Lys	Met	Ser	Phe	Lys	Asp	Val	Tyr	Leu	Val
				100				105					110		
Tyr	Glu	Leu	Met	Asp	Thr	Asp	Leu	His	Gln	Ile	Ile	Lys	Ser	Ser	Gln
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Arg	Leu	Ser	Asn	Asp	His	Cys	Gln	Tyr	Phe	Leu	Phe	Gln	Leu	Leu	Arg
				130				135				140			
Gly	Leu	Lys	Tyr	Ile	His	Ser	Ala	Asn	Ile	Leu	His	Arg	Asp	Leu	Lys
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Pro	Gly	Asn	Leu	Leu	Val	Asn	Ala	Asn	Cys	Asp	Leu	Lys	Ile	Cys	Asp
				165				170				175			
Phe	Gly	Leu	Ala	Arg	Ala	Ser	Asn	Thr	Lys	Gly	Gln	Phe	Met	Thr	Glu
				180				185				190			
Tyr	Val	Val	Thr	Arg	Trp	Tyr	Arg	Ala	Pro	Glu	Leu	Leu	Cys	Cys	
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Asp	Asn	Tyr	Gly	Thr	Ser	Ile	Asp	Val	Trp	Ser	Val	Gly	Cys	Ile	Phe
				210				215			220				
Ala	Glu	Leu	Leu	Gly	Arg	Lys	Pro	Ile	Phe	Gln	Gly	Thr	Glu	Cys	Leu
				225				230			235		240		
Asn	Gln	Leu	Lys	Leu	Ile	Val	Asn	Ile	Ile	Gly	Ser	Gln	Arg	Glu	Glu
				245				250				255			
Asp	Leu	Glu	Phe	Ile	Val	Asn	Pro	Lys	Ala	Lys	Arg	Tyr	Ile	Arg	Ser
				260				265				270			
Leu	Pro	Tyr	Ser	Pro	Gly	Met	Ser	Leu	Ser	Arg	Leu	Tyr	Pro	Cys	Ala
				275				280				285			
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				290				295				300			
Ser	Lys	Arg	Ile	Ser	Ala	Ser	Glu	Ala	Leu	Gln	His	Pro	Tyr	Met	Ala

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Pro Leu Tyr Asp Pro Asn Ala Asn Pro Pro Ala Gln Val Pro Ile Asp			
325		330	335
Leu Asp Val Asp Glu Asp Leu Arg Glu Glu Met Ile Arg Glu Met Ile			
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Trp Asn Glu Met Leu His Tyr His Pro Gln Ala Ser Thr Leu Asn Thr			
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gcg aag acg atg gct	aac aag gac	aaa gac aag gac aag aag aaa	100
Ala Lys Thr Met Ala Ala Asn Lys Asp Lys Asp Lys Asp Lys Lys Lys			
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ccc atc tct cgc tct	gct cgt gct	ggt att cag ttt cca gtt gga cga	148
Pro Ile Ser Arg Ser Ala Arg Ala Gly Ile Gln Phe Pro Val Gly Arg			
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att cac agg caa ctg aag acc	cga gtc tcg gca cat	ggc aga gtt ggt	196
Ile His Arg Gln Leu Lys Thr Arg Val Ser Ala His Gly Arg Val Gly			
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gcc act gca gcc gtc tac aca	gct tca atc ctg gag tat	ctg aca gca	244
Ala Thr Ala Ala Val Tyr Thr Ala Ser Ile Leu Glu Tyr Leu Thr Ala			
60	65	70	75
gag gtt ctt gag ttg gct	ggg aat gcg agc aag gat	ctc aaa gtg aag	292
Glu Val Leu Glu Leu Ala Gly Asn Ala Ser Lys Asp Leu Lys Val Lys			
80	85	90	
agg ata acg cca agg cat	ctg cag ttg gcg att	aga gga gat gag gag	340
Arg Ile Thr Pro Arg His Leu Gln Leu Ala Ile Arg Gly Asp Glu Glu			
95	100	105	
ctg gac aca ctc atc aag gga acg att	gct gga ggt ggt gtg atc cct		388
Leu Asp Thr Leu Ile Lys Gly Thr Ile Ala Gly Gly Val Ile Pro			
110	115	120	

cac atc cac aag tct ctc atc aac aaa acc acc aag gag tga . 430
 His Ile His Lys Ser Leu Ile Asn Lys Thr Thr Lys Glu
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35 40 45

Lys Thr Arg Val Ser Ala His Gly Arg Val Gly Ala Thr Ala Ala Val
50 55 60

Tyr Thr Ala Ser Ile Leu Glu Tyr Leu Thr Ala Glu Val Leu Glu Leu
65 70 75 80

Ala Gly Asn Ala Ser Lys Asp Leu Lys Val Lys Arg Ile Thr Pro Arg
85 90 95

His Leu Gln Leu Ala Ile Arg Gly Asp Glu Glu Leu Asp Thr Leu Ile
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Tyr	Asp	Pro	Leu	His	Gln	Lys	Met	Tyr	Thr	Leu	Asn	Leu	Pro	Glu	Leu		
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gcc	aaa	tct	acg	gtt	tgt	tac	tca	aga	gat	gga	tgg	tta	cta	atg	cgt		145
Ala	Lys	Ser	Thr	Val	Cys	Tyr	Ser	Arg	Asp	Gly	Trp	Leu	Leu	Met	Arg		
30								35							40		
aaa	acc	att	tca	aga	gaa	atg	ttc	ttc	ttc	aac	ccg	ttt	act	cgt	gag		193
Lys	Thr	Ile	Ser	Arg	Glu	Met	Phe	Phe	Phe	Asn	Pro	Phe	Thr	Arg	Glu		
45								50							55		60
ctc	ata	aac	gta	cca	aaa	tgt	act	tta	tca	tat	gat	gcg	atc	gct	ttc		241
Leu	Ile	Asn	Val	Pro	Lys	Cys	Thr	Leu	Ser	Tyr	Asp	Ala	Ile	Ala	Phe		
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tct	tgt	gca	cct	aca	tca	ggt	act	tgc	gtg	ttg	cta	gca	ttt	aag	cat		289
Ser	Cys	Ala	Pro	Thr	Ser	Gly	Thr	Cys	Val	Leu	Leu	Ala	Phe	Lys	His		
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gtt	tcg	tat	cgt	atc	acc	act	acg	act	tgc	cat	ccc	aaa	gca	acc			337
Val	Ser	Tyr	Arg	Ile	Thr	Thr	Thr	Ser	Thr	Cys	His	Pro	Lys	Ala	Thr		
95								100							105		
gag	tgg	gtt	act	gag	gat	cta	caa	ttc	cat	cgt	cgc	ttc	cgc	agt	gaa		385
Glu	Trp	Val	Thr	Glu	Asp	Leu	Gln	Phe	His	Arg	Arg	Phe	Arg	Ser	Glu		
110								115							120		
aca	ctt	aac	cac	agc	aat	gtt	gtc	tat	gcc	aaa	cgt	cgc	ttc	tat	tgc		433
Thr	Leu	Asn	His	Ser	Asn	Val	Val	Tyr	Ala	Lys	Arg	Arg	Phe	Tyr	Cys		
125								130							135		140
ctt	gac	ggt	caa	gga	agc	tta	tat	tac	ttt	gat	ccg	tct	tct	cga	aga		481
Leu	Asp	Gly	Gln	Gly	Ser	Leu	Tyr	Tyr	Phe	Asp	Pro	Ser	Ser	Arg	Arg		
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tgg	gat	ttt	agt	tac	acc	tat	tta	ctg	cca	tgt	cct	tat	atc	tcg	gat		529
Trp	Asp	Phe	Ser	Tyr	Thr	Tyr	Leu	Leu	Pro	Cys	Pro	Tyr	Ile	Ser	Asp		
160								165							170		
aga	ttt	agt	tac	cag	tat	gag	cgg	aag	aag	aga	att	ttc	ttg	gct			577
Arg	Phe	Ser	Tyr	Gln	Tyr	Glu	Arg	Lys	Lys	Lys	Arg	Ile	Phe	Leu	Ala		
175								180							185		
gtg	cg	aaa	gga	gtg	ttc	ttt	aag	ata	ttt	aca	tgt	gat	gg	gag	aag		625
Val	Arg	Lys	Gly	Val	Phe	Phe	Lys	Ile	Phe	Thr	Cys	Asp	Gly	Glu	Lys		
190								195							200		
ccg	ata	gtg	cat	aag	tta	gaa	gat	atc	aat	tgg	gag	gag	atc	aat	agt		673
Pro	Ile	Val	His	Lys	Leu	Glu	Asp	Ile	Asn	Trp	Glu	Glu	Ile	Asn	Ser		
205								210							215		220
act	acg	att	gat	gga	ttg	aca	atc	ttt	acg	gg	ctt	tat	tcc	tct	gag		721
Thr	Thr	Ile	Asp	Gly	Leu	Thr	Ile	Phe	Thr	Gly	Leu	Tyr	Ser	Ser	Glu		
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gtg	aga	ctt	aat	cta	cca	tgg	atg	agg	aat	agt	gtt	tac	ttt	cct	aga		769

Val Arg Leu Asn Leu Pro Trp Met Arg Asn Ser Val Tyr Phe Pro Arg			
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Leu Arg Phe Asn Val Lys Arg Cys Val Ser Tyr Ser Leu Asp Glu Glu			
255	260	265	
agg tat tat ccg cgg aag cag tgg caa gaa cag gag gat tta tgt cct		865	
Arg Tyr Tyr Pro Arg Lys Gln Trp Gln Glu Gln Asp Leu Cys Pro			
270	275	280	
att gag aat ctt tgg att agg cca ccg aag aaa gct gta gat ttc atg		913	
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Val Cys Tyr Ser Arg Asp Gly Trp Leu Leu Met Arg Lys Thr Ile Ser			
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Arg Glu Met Phe Phe Asn Pro Phe Thr Arg Glu Leu Ile Asn Val			
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Pro Lys Cys Thr Leu Ser Tyr Asp Ala Ile Ala Phe Ser Cys Ala Pro			
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Thr Ser Gly Thr Cys Val Leu Leu Ala Phe Lys His Val Ser Tyr Arg			
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Ile Thr Thr Ser Thr Cys His Pro Lys Ala Thr Glu Trp Val Thr			
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Glu Asp Leu Gln Phe His Arg Arg Phe Arg Ser Glu Thr Leu Asn His			
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Ser Asn Val Val Tyr Ala Lys Arg Arg Phe Tyr Cys Leu Asp Gly Gln			
130	135	140	
Gly Ser Leu Tyr Tyr Phe Asp Pro Ser Ser Arg Arg Trp Asp Phe Ser			
145	150	155	160
Tyr Thr Tyr Leu Leu Pro Cys Pro Tyr Ile Ser Asp Arg Phe Ser Tyr			
165	170	175	

Gln Tyr Glu Arg Lys Lys Lys Arg Ile Phe Leu Ala Val Arg Lys Gly
180 185 190

Val Phe Phe Lys Ile Phe Thr Cys Asp Gly Glu Lys Pro Ile Val His
195 200 205

Lys Leu Glu Asp Ile Asn Trp Glu Glu Ile Asn Ser Thr Thr Ile Asp
210 215 220

Gly Leu Thr Ile Phe Thr Gly Leu Tyr Ser Ser Glu Val Arg Leu Asn
225 230 235 240

Leu Pro Trp Met Arg Asn Ser Val Tyr Phe Pro Arg Leu Arg Phe Asn
245 250 255

Val Lys Arg Cys Val Ser Tyr Ser Leu Asp Glu Glu Arg Tyr Tyr Pro
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gatacctaaa ccaaatccaa ttca atg gcg gaa gaa gca aaa tcc aaa gga Met Ala Glu Glu Ala Lys Ser Lys Gly	1 5	171
aac gca gct ttc tct tcc ggc gat tac gcc acc gca ata acc cat ttc Asn Ala Ala Phe Ser Ser Gly Asp Tyr Ala Thr Ala Ile Thr His Phe	10 15 20 25	219
aca gaa gca atc aac ctt tca cca acc aat cac atc ctc tac tca aac Thr Glu Ala Ile Asn Leu Ser Pro Thr Asn His Ile Leu Tyr Ser Asn	30 35 40	267
aga tcc gct tct tac gct tct ctc cac cgt tac gaa gaa gct tta tca Arg Ser Ala Ser Tyr Ala Ser Leu His Arg Tyr Glu Glu Ala Leu Ser	45 50 55	315
gac gcg aag aag act ata gag ctt aaa cct gat tgg tct aaa gga tat Asp Ala Lys Lys Thr Ile Glu Leu Lys Pro Asp Trp Ser Lys Gly Tyr	60 65 70	363
agc cga tta ggt gct gcg ttt att gga ttg tcc aag ttt gat gaa gcg Ser Arg Leu Gly Ala Ala Phe Ile Gly Leu Ser Lys Phe Asp Glu Ala	75 80 85	411
gtt gat tcg tat aag aaa gga tta gag att gat ccg agt aat gag atg Val Asp Ser Tyr Lys Lys Gly Leu Glu Ile Asp Pro Ser Asn Glu Met	90 95 100 105	459
ctt aaa tcg gga tta gct gat gct tcg aga tct agg gtt tcg tca aag Leu Lys Ser Gly Leu Ala Asp Ala Ser Arg Ser Arg Val Ser Ser Lys	110 115 120	507
tcg aat cct ttt gtt gat gcg ttt caa ggg aag gag atg tgg gag aag Ser Asn Pro Phe Val Asp Ala Phe Gln Gly Lys Glu Met Trp Glu Lys	125 130 135	555
ttg acg gcg gat ccg ggg act agg gtt tat ttg gag cag gat gat ttt Leu Thr Ala Asp Pro Gly Thr Arg Val Tyr Leu Glu Gln Asp Asp Phe	140 145 150	603
gtt aag acg atg aag gag att cag agg aac cct aat aat ctt aat ttg Val Lys Thr Met Lys Glu Ile Gln Arg Asn Pro Asn Asn Leu Asn Leu	155 160 165	651
tat atg aag gat aag aga gtt atg aag gct tta ggg gtt ttg ttg aat Tyr Met Lys Asp Lys Arg Val Met Lys Ala Leu Gly Val Leu Leu Asn	170 175 180 185	699
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gat gag agg aaa gag cct gaa ccg gag atg gaa cct atg gag ttg acg Asp Glu Arg Lys Glu Pro Glu Pro Glu Met Glu Pro Met Glu Leu Thr	205 210 215	795
gag gag gag agg cag aag aag gag aga aag gag aag gct ttg aag gag		843

20

Glu Glu Glu Arg Gln Lys Lys Glu Arg Lys Glu Lys Ala Leu Lys Glu
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 235 240 245

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 Val Glu His Tyr Thr Lys Ala Met Glu Leu Asp Asp Glu Asp Ile Ser
 250 255 260 265

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 320 325 330

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 335 340 345

gat gct gag aaa gtc aag aaa gag ctg gag caa cag gag tac ttt gat 1696
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 350 355 360 365

cct acg ata gcc gag gag gag cga gag aaa g gtatatac tgatcctcag 1747
 Pro Thr Ile Ala Glu Glu Glu Arg Glu Lys G
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203

Val Gln Val Arg
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Ile Gly Leu Ser Lys Phe Asp Glu Ala Val Asp Ser Tyr Lys Lys Gly
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Leu Glu Ile Asp Pro Ser Asn Glu Met Leu Lys Ser Gly Leu Ala Asp
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Ala Ser Arg Ser Arg Val Ser Ser Lys Ser Asn Pro Phe Val Asp Ala
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Phe Gln Gly Lys Glu Met Trp Glu Lys Leu Thr Ala Asp Pro Gly Thr
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Arg Val Tyr Leu Glu Gln Asp Asp Phe Val Lys Thr Met Lys Glu Ile
 145 150 155 160

Gln Arg Asn Pro Asn Asn Leu Asn Leu Tyr Met Lys Asp Lys Arg Val
 165 170 175

Met Lys Ala Leu Gly Val Leu Leu Asn Val Lys Phe Gly Gly Ser Ser
 180 185 190

Gly Glu Asp Thr Glu Met Lys Glu Ala Asp Glu Arg Lys Glu Pro Glu
 195 200 205

Pro Glu Met Glu Pro Met Glu Leu Thr Glu Glu Glu Arg Gln Lys Lys
 210 215 220

Glu Arg Lys Glu Lys Ala Leu Lys Glu Lys Gly Glu Gly Asn Val Ala

264

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260	265	270	
Val Tyr Leu Glu Met Gly Lys Tyr Glu Glu Cys Ile Glu Asp Cys Asp			
275	280	285	
Lys Ala Val Glu Arg Gly Arg Glu Leu Arg Ser Asp Phe Lys Met Ile			
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Cys Ser Lys Asp Phe Glu Pro Ala Ile Glu Thr Phe Gln Lys Ala Leu			
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Thr Glu His Arg Asn Pro Asp Thr Leu Lys Lys Leu Asn Asp Ala Glu			
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Lys Val Lys Lys Glu Leu Glu Gln Gln Glu Tyr Phe Asp Pro Thr Ile			
355	360	365	
Ala Glu Glu Glu Arg Glu Lys Gly Asn Gly Phe Phe Lys Glu Gln Lys			
370	375	380	
Tyr Pro Glu Ala Val Lys His Tyr Ser Glu Ala Ile Lys Arg Asn Pro			
385	390	395	400
Asn Asp Val Arg Ala Tyr Ser Asn Arg Ala Ala Cys Tyr Thr Lys Leu			
405	410	415	
Gly Ala Leu Pro Glu Gly Leu Lys Asp Ala Glu Lys Cys Ile Glu Leu			
420	425	430	
Asp Pro Ser Phe Thr Lys Gly Tyr Ser Arg Lys Gly Ala Ile Gln Phe			
435	440	445	
Phe Met Lys Glu Tyr Asp Lys Ala Met Glu Thr Tyr Gln Glu Gly Leu			
450	455	460	
Lys His Asp Pro Lys Asn Gln Glu Phe Leu Asp Gly Val Arg Arg Cys			
465	470	475	480
Val Glu Gln Ile Asn Lys Ala Ser Arg Gly Asp Leu Thr Pro Glu Glu			
485	490	495	
Leu Lys Glu Arg Gln Ala Lys Ala Met Gln Asp Pro Glu Val Gln Asn			
500	505	510	
Ile Leu Ser Asp Pro Val Met Arg Gln Val Leu Val Asp Phe Gln Glu			
515	520	525	
Asn Pro Lys Ala Ala Gln Glu His Met Lys Asn Pro Met Val Met Asn			

530

535

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 atcaagaaa atg gga aga gca ccg tgt tgt gat aag gcc aac gtg aag aaa 171
 Met Gly Arg Ala Pro Cys Cys Asp Lys Ala Asn Val Lys Lys
 1 5 10

ggg cct tgg tct cct gag gaa gac gcc aaa ctc aaa gat tac atc gag 219
 Gly Pro Trp Ser Pro Glu Glu Asp Ala Lys Leu Lys Asp Tyr Ile Glu
 15 20 25 30

aat agt ggc aca gga ggc aac tgg att gct ttg cct cag aaa att g 265
 Asn Ser Gly Thr Gly Gly Asn Trp Ile Ala Leu Pro Gln Lys Ile G
 35 40 45

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gt tta agg aga tgt ggg aag agt tgc agg cta agg tgg ctc aac tat 432
 ly Leu Arg Arg Cys Gly Lys Ser Cys Arg Leu Arg Trp Leu Asn Tyr
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 Leu Arg Pro Asn Ile Lys His Gly Gly Phe Ser Glu Glu Asp Asn
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 Ile Ile Cys Asn Leu Tyr Val Thr Ile Gly Ser Ar
 80 85

206

27

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Phe Ile Asn Asn Asn Asn Ile Val Asn Leu Glu Thr Ile Glu Asn		
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aca aaa gtc tat gga gac gcc tca gta gcc gga gcc gct gtc cga gca		1360
Thr Lys Val Tyr Gly Asp Ala Ser Val Ala Gly Ala Ala Val Arg Ala		
320	325	330
335		
gct ttg ggc gga ggg aca acg agt aca tcg gcg gat caa agt aca ata		1408
Ala Leu Gly Gly Thr Thr Ser Thr Ala Asp Gln Ser Thr Ile		
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agt tgg gag gat ata act tct cta gtt aat tcc gaa gat gca agt tac		1456
Ser Trp Glu Asp Ile Thr Ser Leu Val Asn Ser Glu Asp Ala Ser Tyr		
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Phe Asn Ala Pro Asn His Val		
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Gly Thr Gly Gly Asn Trp Ile Ala Leu Pro Gln Lys Ile Gly Leu Arg		
35	40	45
Arg Cys Gly Lys Ser Cys Arg Leu Arg Trp Leu Asn Tyr Leu Arg Pro		
50	55	60
Asn Ile Lys His Gly Gly Phe Ser Glu Glu Asp Asn Ile Ile Cys		
65	70	75
		80
Asn Leu Tyr Val Thr Ile Gly Ser Arg Trp Ser Ile Ile Ala Ala Gln		
85	90	95
Leu Pro Gly Arg Thr Asp Asn Asp Ile Lys Asn Tyr Trp Asn Thr Arg		
100	105	110
Leu Lys Lys Lys Leu Leu Asn Lys Gln Arg Lys Glu Phe Gln Glu Ala		
115	120	125
Arg Met Lys Gln Glu Met Val Met Met Lys Arg Gln Gln Gln Gly Gln		
130	135	140

Gly Gln Gly Gln Ser Asn Gly Ser Thr Asp Leu Tyr Leu Asn Asn Met
 145 150 155 160
 Phe Gly Ser Ser Pro Trp Pro Leu Leu Pro Gln Leu Pro Pro Pro His
 165 170 175
 His Gln Ile Pro Leu Gly Met Met Glu Pro Thr Ser Cys Asn Tyr Tyr
 180 185 190
 Gln Thr Thr Pro Ser Cys Asn Leu Glu Gln Lys Pro Leu Ile Thr Leu
 195 200 205
 Lys Asn Met Val Lys Ile Glu Glu Glu Gln Glu Arg Thr Asn Pro Asp
 210 215 220
 His His His Gln Asp Ser Val Thr Asn Pro Phe Asp Phe Ser Phe Ser
 225 230 235 240
 Gln Leu Leu Leu Asp Pro Asn Tyr Tyr Leu Gly Ser Gly Gly Gly
 245 250 255
 Glu Gly Asp Phe Ala Ile Met Ser Ser Ser Thr Asn Ser Pro Leu Pro
 260 265 270
 Asn Thr Ser Ser Asp Gln His Pro Ser Gln Gln Gln Glu Ile Leu Gln
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 Trp Phe Gly Ser Ser Asn Phe Gln Thr Glu Ala Ile Asn Asp Met Phe
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 Ile Asn Asn Asn Asn Ile Val Asn Leu Glu Thr Ile Glu Asn Thr
 305 310 315 320
 Lys Val Tyr Gly Asp Ala Ser Val Ala Gly Ala Ala Val Arg Ala Ala
 325 330 335
 Leu Gly Gly Gly Thr Thr Ser Thr Ser Ala Asp Gln Ser Thr Ile Ser
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 Asn Ala Pro Asn His Val
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										5

 ggt tct tct gtg gca aag ctt gcc ata aga agg aca ctg tct cag tct 103

Gly	Ser	Ser	Val	Ala	Lys	Leu	Ala	Ile	Arg	Arg	Thr	Leu	Ser	Gln	Ser

 10 15 20

cgt tgt ggt tca tat gcc act aga aca agg gtt ttg cct tgt caa acc 151

Arg	Cys	Gly	Ser	Tyr	Ala	Thr	Arg	Thr	Arg	Val	Leu	Pro	Cys	Gln	Thr

 25 30 35

aga tgt ttt cac tct aca ata ctc aaa tca aag gca gag tct gct gca 199

Arg	Cys	Phe	His	Ser	Thr	Ile	Leu	Lys	Ser	Lys	Ala	Glu	Ser	Ala	Ala

 40 45 50

cct gtt cca cgt cct gtc cca ctt tct aag cta act gat agc ttc tta 247

Pro	Val	Pro	Arg	Pro	Val	Pro	Leu	Ser	Lys	Leu	Thr	Asp	Ser	Phe	Leu

 55 60 65 70

gat gga aca agc agt gtg tat cta gag gag tta caa aga gct tgg gac 295

Asp	Gly	Thr	Ser	Val	Tyr	Leu	Glu	Glu	Leu	Gln	Arg	Ala	Trp	Glu

 75 80 85

gct gat ccc aac agt gtt gat gag tcg tgg gat aac ttt ttt agg aat 343

Ala	Asp	Pro	Asn	Ser	Val	Asp	Glu	Ser	Trp	Asp	Asn	Phe	Phe	Arg	Asn

 90 95 100

ttt gtg ggt cag gct tct aca tcg cct ggt atc tcg ggg caa acc att 391

Phe	Val	Gly	Gln	Ala	Ser	Thr	Ser	Pro	Gly	Ile	Ser	Gly	Gln	Thr	Ile

 105 110 115

caa gaa agc atg cgt ttg ttg cta gtt aga gct tac cag gtt aat 439

Gln Glu Ser Met Arg Leu Leu Leu Val Arg Ala Tyr Gln Val Asn			
120	125	130	
ggc cac atg aag gcc aag ctt gat cct tta ggt cta gag aag aga gag			487
Gly His Met Lys Ala Lys Leu Asp Pro Leu Gly Leu Glu Lys Arg Glu			
135	140	145	150
att cca gag gat ctc acg cca ggt ctt tat ggg ttt act gag gct gat			535
Ile Pro Glu Asp Leu Thr Pro Gly Leu Tyr Gly Phe Thr Glu Ala Asp			
155	160	165	
ctt gat cgg gaa ttc ttt ctg ggt gta tgg agg atg tcg ggt ttt ctc			583
Leu Asp Arg Glu Phe Leu Gly Val Trp Arg Met Ser Gly Phe Leu			
170	175	180	
tct gag aac cgc ccg gtt caa aca ctg agg tcg ata ctg tcg agg ctt			631
Ser Glu Asn Arg Pro Val Gln Thr Leu Arg Ser Ile Leu Ser Arg Leu			
185	190	195	
gag caa gct tac tgt ggg act ata ggg tat gag tac atg cac att gct			679
Glu Gln Ala Tyr Cys Gly Thr Ile Gly Tyr Glu Tyr Met His Ile Ala			
200	205	210	
gat agg gat aaa tgt aac tgg ttg aga gac aag atc gag acc cca act			727
Asp Arg Asp Lys Cys Asn Trp Leu Arg Asp Lys Ile Glu Thr Pro Thr			
215	220	225	230
cct cga cag tac aat agt gag cgt cgg atg gtt att tat gat agg ctt			775
Pro Arg Gln Tyr Asn Ser Glu Arg Arg Met Val Ile Tyr Asp Arg Leu			
235	240	245	
acc tgg agc aca cag ttt gag aat ttc ttg gct act aag tgg acc acg			823
Thr Trp Ser Thr Gln Phe Glu Asn Phe Leu Ala Thr Lys Trp Thr Thr			
250	255	260	
gct aaa agg ttt gga ctg gaa ggt gct gaa tct ttg att cct ggc atg			871
Ala Lys Arg Phe Gly Leu Glu Gly Ala Glu Ser Leu Ile Pro Gly Met			
265	270	275	
aag gag atg ttc gat agg tct gca gat ctc ggg gta gag aac ata gtt			919
Lys Glu Met Phe Asp Arg Ser Ala Asp Leu Gly Val Glu Asn Ile Val			
280	285	290	
atc ggt atg ccc cat agg ggt cga ctt aat gtt ttg ggt aat gtt gtt			967
Ile Gly Met Pro His Arg Gly Arg Leu Asn Val Leu Gly Asn Val Val			
295	300	305	310
aga aaa cct cta cgc caa ata ttc agc gag ttt agc ggt ggt act agg			1015
Arg Lys Pro Leu Arg Gln Ile Phe Ser Glu Phe Ser Gly Gly Thr Arg			
315	320	325	
cca gta gat gaa gtt ggg ctt tac acc gga aca ggt gat gtg aaa tac			1063
Pro Val Asp Glu Val Gly Leu Tyr Thr Gly Thr Gly Asp Val Lys Tyr			
330	335	340	
cac ttg ggt aca tct tat gat cgt cca act aga gga ggc aaa cat ctc			1111
His Leu Gly Thr Ser Tyr Asp Arg Pro Thr Arg Gly Gly Lys His Leu			

345	350	355	
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gtt gtg ata ggt aaa acc aga gcg aaa caa tat tac acg aaa gac gag Val Val Ile Gly Lys Thr Arg Ala Lys Gln Tyr Tyr Thr Lys Asp Glu 375	380	385	1207
aac aga aca aag aac atg ggt att ttg atc cat ggg gat ggt agc ttt Asn Arg Thr Lys Asn Met Gly Ile Leu Ile His Gly Asp Gly Ser Phe 395	400	405	1255
gcc gga caa gga gtg gtg tat gaa act ctc cat ctt agt gca ctt cct Ala Gly Gln Gly Val Val Tyr Glu Thr Leu His Leu Ser Ala Leu Pro 410	415	420	1303
aac tac tgt acc ggt gga aca gtg cac att gtg gtg aat aat caa gtg Asn Tyr Cys Thr Gly Gly Thr Val His Ile Val Val Asn Asn Gln Val 425	430	435	1351
gct ttc aca acc gat ccc agg gaa gga agg tct tca cag tat tgc act Ala Phe Thr Thr Asp Pro Arg Glu Gly Arg Ser Ser Gln Tyr Cys Thr 440	445	450	1399
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gac att gaa gca gta gtg cat gct tgt gag ctt gct gct gag tgg cgc Asp Ile Glu Ala Val Val His Ala Cys Glu Leu Ala Ala Glu Trp Arg 475	480	485	1495
cag acg ttc cat tct gat gtt gtt gat tta gta tgc tac cgt cgc Gln Thr Phe His Ser Asp Val Val Asp Leu Val Cys Tyr Arg Arg 490	495	500	1543
ttt ggg cat aac gag ata gac gaa ccg tca ttc aca caa cca aaa atg Phe Gly His Asn Glu Ile Asp Glu Pro Ser Phe Thr Gln Pro Lys Met 505	510	515	1591
tac aag gtctggctat tataatcatcc atctctgtga aataatctaa taaccaattc Tyr Lys 520			1647
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tggtgatag gtg ata cgc agt cat ccc tcg tca ctt caa atc tac cag gag Val Ile Arg Ser His Pro Ser Ser Leu Gln Ile Tyr Gln Glu 525	530		1758
aag ctc ttg caa tct gga cag gta acc caa gaa gat att gat aag att Lys Leu Leu Gln Ser Gly Gln Val Thr Gln Glu Asp Ile Asp Lys Ile 535	540	545	1806
caa aag aaa gta agc tct atc ctc aat gaa gaa tat gag gca agt aaa			1854

Gln Lys Lys Val Ser Ser Ile Leu Asn Glu Glu Tyr Glu Ala Ser Lys
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 Asp Tyr Ile Pro Gln Lys Arg Asp Trp Leu Ala Ser His Trp Thr Gly
 570 575 580
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 Phe Lys Ser Pro Glu Gln Ile Ser Arg Ile Arg Asn Thr Gl
 585 590 595
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 y Val Lys Pro Glu Ile
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 Pro His Arg Gly Val Lys Arg Val Tyr Glu Gln Arg Ala Gln Met Ile
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 Glu Ser Gly Glu Gly Ile Asp Trp Gly Leu Gly Glu Ala Leu Ala Phe
 635 640 645
 gct aca ctg gtt gtg gaa ggg aac cat gtt cgg cta agt ggt caa gat 2259
 Ala Thr Leu Val Val Glu Gly Asn His Val Arg Leu Ser Gly Gln Asp
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 gtt gaa aga gga act ttc agt cat aga cac tca gtg ctt cat gat caa 2307
 Val Glu Arg Gly Thr Phe Ser His Arg His Ser Val Leu His Asp Gln
 670 675 680
 gaa acc ggg gag gaa tat tgt ccc ctc gat cac cta atc aaa aac caa 2355
 Glu Thr Gly Glu Tyr Cys Pro Leu Asp His Leu Ile Lys Asn Gln
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 700 705
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 710 715 720
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 r Met Glu Asn Pro Asn Ser Leu Val Ile Trp Glu Ala Gln Phe Gly As
 725 730 735
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755	760	765	770
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775	780	785	
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795	800	805	
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835	840	845	
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850	855	860	
865			
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 Gly Phe Thr Glu Ala Asp Leu Asp Arg Glu Phe Phe Leu Gly Val Trp
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 370 375 380
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 405 410 415
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 435 440 445

Ser Ser Gln Tyr Cys Thr Asp Val Ala Lys Ala Leu Ser Ala Pro Ile
 450 455 460
 Phe His Val Asn Ala Asp Asp Ile Glu Ala Val Val His Ala Cys Glu
 465 470 475 480
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 485 490 495
 Leu Val Cys Tyr Arg Arg Phe Gly His Asn Glu Ile Asp Glu Pro Ser
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 Phe Thr Gln Pro Lys Met Tyr Lys Val Ile Arg Ser His Pro Ser Ser
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 545 550 555 560
 Glu Tyr Glu Ala Ser Lys Asp Tyr Ile Pro Gln Lys Arg Asp Trp Leu
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 Ala Ser His Trp Thr Gly Phe Lys Ser Pro Glu Gln Ile Ser Arg Ile
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 Arg Asn Thr Gly Val Lys Pro Glu Ile Leu Lys Asn Val Gly Lys Ala
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 Ile Ser Thr Phe Pro Glu Asn Phe Lys Pro His Arg Gly Val Lys Arg
 610 615 620
 Val Tyr Glu Gln Arg Ala Gln Met Ile Glu Ser Gly Glu Gly Ile Asp
 625 630 635 640
 Trp Gly Leu Gly Glu Ala Leu Ala Phe Ala Thr Leu Val Val Glu Gly
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 Asn His Val Arg Leu Ser Gly Gln Asp Val Glu Arg Gly Thr Phe Ser
 660 665 670
 His Arg His Ser Val Leu His Asp Gln Glu Thr Gly Glu Glu Tyr Cys
 675 680 685
 Pro Leu Asp His Leu Ile Lys Asn Gln Asp Pro Glu Met Phe Thr Val
 690 695 700
 Ser Asn Ser Ser Leu Ser Glu Phe Gly Val Leu Gly Phe Glu Leu
 705 710 715 720
 Gly Tyr Ser Met Glu Asn Pro Asn Ser Leu Val Ile Trp Glu Ala Gln
 725 730 73
 Phe Gly Ap Phe Ala Asn Gly Ala Gln Val Met Phe Asp Gln Phe Ile
 740 745 750

Ser Ser Gy Glu Ala Lys Trp Leu Arg Gln Thr Gly Leu Val Val Leu
 755 760 765

Leu Pro Hs Gly Tyr Asp Gly Gln Gly Pro Glu His Ser Ser Gly Arg
 770 775 780

Leu Glu Ag Phe Leu Gln Met Ser Asp Asp Asn Pro Tyr Val Ile Pro
 785 790 795

Glu Met Asp Pro Thr Leu Arg Lys Gln Ile Gln Glu Cys Asn Trp Gln
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Val Val Asn Val Thr Thr Pro Ala Asn Trp Phe His Val Leu Arg Arg
 815 820 825

Gln Ile His Arg Asp Phe Arg Lys Pro Leu Ile Val Met Ala Pro Lys
 830 835 840

Asn Leu Leu Arg His Lys Gln Cys Val Ser Asn Leu Ser Glu Phe Asp
 845 850 855

Asp Val Lys Gly His Pro Gly Phe Asp Lys Gln Gly Thr Arg Phe Lys
 860 865 870

Arg Leu Ile Lys Asp Gln Ser Gly His Ser Asp Leu Glu Glu
 875 880 885

Asp Ala Glu Ile Val Trp Cys Gln Glu Glu Pro Met Asn Met Gly Gly
 890 895 900

Tyr Gln Tyr Ile Ala Leu Arg Leu Cys Thr Ala Met Lys Ala Leu Gln
 905 910 915

Arg Gly Asn Phe Asn Asp Ile Lys Tyr Val Gly Arg Leu Pro Ser Ala
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Met Phe Ile Arg Val Ser Ala Arg Pro	
1	5

gcg aca ttc gtc gag gat ttc aaa gcc gcc tgg tcg gaa tct cac atc	99
Ala Thr Phe Val Glu Asp Phe Lys Ala Ala Trp Ser Glu Ser His Ile	
10	15
15	20
20	25

cgt caa atg gaa gac gga aaa gct atc cag ctc gtc ctt gat cag agc	147
Arg Gln Met Glu Asp Gly Lys Ala Ile Gln Leu Val Leu Asp Gln Ser	
30	35
35	40

act g gtacaccaac gccacagtta tattttaaa cgaaaaacatt ttgaaaattaa	201
Thr G	

tgggtttttt atgtaatata ctctcactgt acatgttcat atttgtcttt taaag ga	258
ly	

tgt gga ttt gct tcc aaa aga aaa tat cta ttc gga cga gtg agc atg	306
Cys Gly Phe Ala Ser Lys Arg Lys Tyr Leu Phe Gly Arg Val Ser Met	
45	50
50	55

aag atc aaa ctc att ccc gga gac tct gcc ggt acg gtc acc gct ttc	354
Lys Ile Lys Leu Ile Pro Gly Asp Ser Ala Gly Thr Val Thr Ala Phe	
60	65
65	70
70	75

tac gtaaggcttat cattttactc cactagttt gaaattttac acattcacac	407
Tyr	

aataaaaaat aacattttct tgaaacacta acggtaaat cattgatatg tctatag	464
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atg aac tcc gat acg gcc acg gtg aga gac gag cta gat ttt gag ttc	512
Met Asn Ser Asp Thr Ala Thr Val Arg Asp Glu Leu Asp Phe Glu Phe	
80	85
85	90

ttg gga aac aga agt ggt caa cct tac tca gtg caa aca aac ata ttt	560
Leu Gly Asn Arg Ser Gly Gln Pro Tyr Ser Val Gln Thr Asn Ile Phe	
95	100
100	105

gct cat ggc aaa gga gat aga gaa caa aga gtt aat ctt tgg ttc gac	608
Ala His Gly Lys Gly Asp Arg Glu Gln Arg Val Asn Leu Trp Phe Asp	
110	115
115	120

cca tct atg gat tac cac act tac act atc tta tgg tca cac aaa cac	656
Pro Ser Met Asp Tyr His Thr Tyr Thr Ile Leu Trp Ser His Lys His	
125	130
130	135
135	140

att gtg taagctttc tctaattgt a ctttcaacta gaatcaacat ttactgttc 712
 Ile Val

aaaacaaaaa atcaccattt actgttaaaa aaaaccttag tttaacgtgg ggttgtttg 772

gttactcagt ttt tac gta gac gat gtg cca ata aga gaa tac aaa aac 821
 Phe Tyr Val Asp Asp Val Pro Ile Arg Glu Tyr Lys Asn
 145 150 155

aac gaa gcc aag aac ata gct tac cca aca tca caa cct atg gga gta 869
 Asn Glu Ala Lys Asn Ile Ala Tyr Pro Thr Ser Gln Pro Met Gly Val
 160 165 170

tac tca aca tta tgg gaa gca gat gac tgg gca aca cgt ggt gga tta 917
 Tyr Ser Thr Leu Trp Glu Ala Asp Asp Trp Ala Thr Arg Gly Gly Leu
 175 180 185

gag aaa att gat tgg agc aaa gct cca ttt tat gct tat tac aaa gat 965
 Glu Lys Ile Asp Trp Ser Lys Ala Pro Phe Tyr Ala Tyr Tyr Lys Asp
 190 195 200

ttc gac atc gaa ggt tgt cct gtt cct gga cca acc ttt tgt cca tcg 1013
 Phe Asp Ile Glu Gly Cys Pro Val Pro Gly Pro Thr Phe Cys Pro Ser
 205 210 215

aac cct cat aat tgg tgg gaa ggt tat gcc tat cag tct ctt aac gcc 1061
 Asn Pro His Asn Trp Trp Glu Gly Tyr Ala Tyr Gln Ser Leu Asn Ala
 220 225 230 235

gtt gaa gct cga cgt tac cgg tgg gtt aga gta aac cat atg gtt tat 1109
 Val Glu Ala Arg Arg Tyr Arg Trp Val Arg Val Asn His Met Val Tyr
 240 245 250

gat tat tgt act gac cgg tct agg ttt cct gtc cca cca ccc gag tgt 1157
 Asp Tyr Cys Thr Asp Arg Ser Arg Phe Pro Val Pro Pro Glu Cys
 255 260 265

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 Arg Ala
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Ala Ile Gln Leu Val Leu Asp Gln Ser Thr Gly Cys Gly Phe Ala Ser
 35 40 45

Lys Arg Lys Tyr Leu Phe Gly Arg Val Ser Met Lys Ile Lys Leu Ile
 50 55 60

Pro Gly Asp Ser Ala Gly Thr Val Thr Ala Phe Tyr Met Asn Ser Asp
 65 70 75 80

Thr Ala Thr Val Arg Asp Glu Leu Asp Phe Glu Phe Leu Gly Asn Arg
 85 90 95

Ser Gly Gln Pro Tyr Ser Val Gln Thr Asn Ile Phe Ala His Gly Lys
 100 105 110

Gly Asp Arg Glu Gln Arg Val Asn Leu Trp Phe Asp Pro Ser Met Asp
 115 120 125

Tyr His Thr Tyr Thr Ile Leu Trp Ser His Lys His Ile Val Phe Tyr
 130 135 140

Val Asp Asp Val Pro Ile Arg Glu Tyr Lys Asn Asn Glu Ala Lys Asn
 145 150 155 160

Ile Ala Tyr Pro Thr Ser Gln Pro Met Gly Val Tyr Ser Thr Leu Trp
 165 170 175

Glu Ala Asp Asp Trp Ala Thr Arg Gly Gly Leu Glu Lys Ile Asp Trp
 180 185 190

Ser Lys Ala Pro Phe Tyr Ala Tyr Tyr Lys Asp Phe Asp Ile Glu Gly
 195 200 205

Cys Pro Val Pro Gly Pro Thr Phe Cys Pro Ser Asn Pro His Asn Trp
 210 215 220

Trp Glu Gly Tyr Ala Tyr Gln Ser Leu Asn Ala Val Glu Ala Arg Arg
 225 230 235 240

Tyr Arg Trp Val Arg Val Asn His Met Val Tyr Asp Tyr Cys Thr Asp
 245 250 255

Arg Ser Arg Phe Pro Val Pro Pro Pro Glu Cys Arg Ala
 260 265

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Met Ala Ser Lys Val Ile Ser Ala Thr
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atc cgc aga acc cta acc aaa cca cac ggc act ttt tcc cgg tgt cgc 99
Ile Arg Arg Thr Leu Thr Lys Pro His Gly Thr Phe Ser Arg Cys Arg
10 15 20 25

tac tta tca acc gcc gct gct gcg acg gag gtg aat tac gag gat gaa 147
Tyr Leu Ser Thr Ala Ala Ala Thr Glu Val Asn Tyr Glu Asp Glu
30 35 40

tcg att atg atg aaa gga gtt cga att tca ggt aga cct ctt tac tta 195
Ser Ile Met Met Lys Gly Val Arg Ile Ser Gly Arg Pro Leu Tyr Leu
45 50 55

gat atg caa gcg acg act ccg att gat cct aga gta ttc gat gcg atg 243
Asp Met Gln Ala Thr Thr Pro Ile Asp Pro Arg Val Phe Asp Ala Met
60 65 70

aat gct tca cag atc cat gag tat ggg aat cct cac tcg cga acg cat 291
Asn Ala Ser Gln Ile His Glu Tyr Gly Asn Pro His Ser Arg Thr His
75 80 85

ctc tac ggc tgg gaa gct gag aac gcc gtc gag aac gca cga aac cag 339
Leu Tyr Trp Glu Ala Glu Asn Ala Val Glu Asn Ala Arg Asn Gln
90 95 100 105

gtc gcg aaa ctg atc gaa gct tca ccg aag gag atc gta ttc gtg tcc 387
Val Ala Lys Leu Ile Glu Ala Ser Pro Lys Glu Ile Val Phe Val Ser
110 115 120

ggt gca acg gag gcg aac aat atg gcg gtg aaa gga gtg atg cac ttt 435
Gly Ala Thr Glu Ala Asn Asn Met Ala Val Lys Gly Val Met His Phe
125 130 135

tac aag gac acg aag aaa cat gtg ata act aca cag act gag cat aag 483
Tyr Lys Asp Thr Lys His Val Ile Thr Thr Gln Thr Glu His Lys
140 145 150

tgt gtg ctt gat tcg tgt agg cat ttg cag caa gaa gga ttt gag gta 531
Cys Val Leu Asp Ser Cys Arg His Leu Gln Gln Glu Gly Phe Glu Val
155 160 165

act tat tta cct gtg aaa act gat gga ttg gtt gat tta gag atg ttg 579
Thr Tyr Leu Pro Val Lys Thr Asp Gly Leu Val Asp Leu Glu Met Leu
170 175 180 185

aga gaa gct att agg cca gac aca ggg cta gtt tct att atg gct gtg 627
Arg Glu Ala Ile Arg Pro Asp Thr Gly Leu Val Ser Ile Met Ala Val
190 195 200

aac aat gag att ggt gtg gtt caa cct atg gag gag att ggt atg att 675
Asn Asn Glu Ile Gly Val Val Gln Pro Met Glu Glu Ile Gly Met Ile
205 210 215

tgc aaa gag cat aat gtt ccg ttt cat act gat gct gct caa gct att		723
Cys Lys Glu His Asn Val Pro Phe His Thr Asp Ala Ala Gln Ala Ile		
220	225	230
ggg aag ata cct gtt gat gtt aag aag tgg aat gtt gct ttg atg tct		771
Gly Lys Ile Pro Val Asp Val Lys Lys Trp Asn Val Ala Leu Met Ser		
235	240	245
atg agt gct cac aag atc tat gga ccg aaa ggt gtt ggt gct ttg tat		819
Met Ser Ala His Lys Ile Tyr Gly Pro Lys Gly Val Gly Ala Leu Tyr		
250	255	265
gtg agg agg agg ccg aga atc agg ctt gag ccg ttg atg aat ggt gga		867
Val Arg Arg Arg Pro Arg Ile Arg Leu Glu Pro Leu Met Asn Gly Gly		
270	275	280
ggt cag gag agg gga ttg cgt agt ggt acg ggg gct acg cag cag att		915
Gly Gln Glu Arg Gly Leu Arg Ser Gly Thr Gly Ala Thr Gln Gln Ile		
285	290	295
gtt ggg ttc ggg gct gct tgt gag ttg gct atg aag gag atg gag tat		963
Val Gly Phe Gly Ala Ala Cys Glu Leu Ala Met Lys Glu Met Glu Tyr		
300	305	310
gat gag aag tgg att aag ggg tta cag gag agg ttg ctg aat ggg gtt		1011
Asp Glu Lys Trp Ile Lys Gly Leu Gln Glu Arg Leu Leu Asn Gly Val		
315	320	325
aga gag aag ctt gat ggt gtt gtg gtg aat ggt tca atg gat agt cga		1059
Arg Glu Lys Leu Asp Gly Val Val Val Asn Gly Ser Met Asp Ser Arg		
330	335	340
345		
tat gta ggg aat ttg aat ttg tcg ttt gct tat gtt gaa gga gag agt		1107
Tyr Val Gly Asn Leu Asn Leu Ser Phe Ala Tyr Val Glu Gly Glu Ser		
350	355	360
ttg ttg atg gga ttg aag gaa gtt gca gtg tct agt gga agt gct tgt		1155
Leu Leu Met Gly Leu Lys Glu Val Ala Val Ser Ser Gly Ser Ala Cys		
365	370	375
act agt gcg agt ttg gag cct tct tat gtg ttg aga gct ttg ggt gtg		1203
Thr Ser Ala Ser Leu Glu Pro Ser Tyr Val Leu Arg Ala Leu Gly Val		
380	385	390
gat gaa gac atg gct cac act tcg att agg ttt ggg att ggt agg ttt		1251
Asp Glu Asp Met Ala His Thr Ser Ile Arg Phe Gly Ile Gly Arg Phe		
395	400	405
acc acg aag gaa gag att gat aaa gcg gtc gag ctt acg gtt aaa caa		1299
Thr Thr Lys Glu Glu Ile Asp Lys Ala Val Glu Leu Thr Val Lys Gln		
410	415	420
425		
gtt gag aag ttg agg gaa atg agc ccg ctt tat gaa atg gtt aaa gaa		1347
Val Glu Lys Leu Arg Glu Met Ser Pro Leu Tyr Glu Met Val Lys Glu		
430	435	440
ggt atc gat atc aag aac att caa tgg tct caa cac tga ttcaacagtt		1396

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 445 450

cca 1399

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 35 40 45

Arg Ile Ser Gly Arg Pro Leu Tyr Leu Asp Met Gln Ala Thr Thr Pro
 50 55 60

Ile Asp Pro Arg Val Phe Asp Ala Met Asn Ala Ser Gln Ile His Glu
 65 70 75 80

Tyr Gly Asn Pro His Ser Arg Thr His Leu Tyr Gly Trp Glu Ala Glu
 85 90 95

Asn Ala Val Glu Asn Ala Arg Asn Gln Val Ala Lys Leu Ile Glu Ala
 100 105 110

Ser Pro Lys Glu Ile Val Phe Val Ser Gly Ala Thr Glu Ala Asn Asn
 115 120 125

Met Ala Val Lys Gly Val Met His Phe Tyr Lys Asp Thr Lys Lys His
 130 135 140

Val Ile Thr Thr Gln Thr Glu His Lys Cys Val Leu Asp Ser Cys Arg
 145 150 155 160

His Leu Gln Gln Glu Gly Phe Glu Val Thr Tyr Leu Pro Val Lys Thr
 165 170 175

Asp Gly Leu Val Asp Leu Glu Met Leu Arg Glu Ala Ile Arg Pro Asp
 180 185 190

Thr Gly Leu Val Ser Ile Met Ala Val Asn Asn Glu Ile Gly Val Val
 195 200 205

Gln Pro Met Glu Glu Ile Gly Met Ile Cys Lys Glu His Asn Val Pro
 210 215 220

Phe His Thr Asp Ala Ala Gln Ala Ile Gly Lys Ile Pro Val Asp Val
 225 230 235 240

Lys Lys Trp Asn Val Ala Leu Met Ser Met Ser Ala His Lys Ile Tyr
 245 250 255
 Gly Pro Lys Gly Val Gly Ala Leu Tyr Val Arg Arg Arg Pro Arg Ile
 260 265 270
 Arg Leu Glu Pro Leu Met Asn Gly Gly Gln Glu Arg Gly Leu Arg
 275 280 285
 Ser Gly Thr Gly Ala Thr Gln Gln Ile Val Gly Phe Gly Ala Ala Cys
 290 295 300
 Glu Leu Ala Met Lys Glu Met Glu Tyr Asp Glu Lys Trp Ile Lys Gly
 305 310 315 320
 Leu Gln Glu Arg Leu Leu Asn Gly Val Arg Glu Lys Leu Asp Gly Val
 325 330 335
 Val Val Asn Gly Ser Met Asp Ser Arg Tyr Val Gly Asn Leu Asn Leu
 340 345 350
 Ser Phe Ala Tyr Val Glu Gly Glu Ser Leu Leu Met Gly Leu Lys Glu
 355 360 365
 Val Ala Val Ser Ser Gly Ser Ala Cys Thr Ser Ala Ser Leu Glu Pro
 370 375 380
 Ser Tyr Val Leu Arg Ala Leu Gly Val Asp Glu Asp Met Ala His Thr
 385 390 395 400
 Ser Ile Arg Phe Gly Ile Gly Arg Phe Thr Thr Lys Glu Glu Ile Asp
 405 410 415
 Lys Ala Val Glu Leu Thr Val Lys Gln Val Glu Lys Leu Arg Glu Met
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act gat ctt cggt cta act cac tcg aac ctc gtc gga gaa att cct gat Thr Asp Leu Arg Leu Thr His Ser Asn Leu Val Gly Glu Ile Pro Asp 225 230 235	721
tcg atc atg aat ctg gtg ttg tta gag aat ctt gat tta gct atg aat Ser Ile Met Asn Leu Val Leu Leu Glu Asn Leu Asp Leu Ala Met Asn 240 245 250	769
agt ctc acc gga gaa ata cct gag agt atc gga aga ctc gaa tcg gtt Ser Leu Thr Gly Glu Ile Pro Glu Ser Ile Gly Arg Leu Glu Ser Val 255 260 265 270	817
tac cag att gag ctc tac gat aac cggt tta tct gga aaa tta ccg gag Tyr Gln Ile Glu Leu Tyr Asp Asn Arg Leu Ser Gly Lys Leu Pro Glu 275 280 285	865
agt atc gga aat tta acc gaa ttg agg aat ttt gat gtc tcg cag aat Ser Ile Gly Asn Leu Thr Glu Leu Arg Asn Phe Asp Val Ser Gln Asn 290 295 300	913
aat cta acc ggt gaa cta ccg gaa aag atc gct gct ctg caa ctt atc Asn Leu Thr Gly Glu Leu Pro Glu Lys Ile Ala Ala Leu Gln Leu Ile 305 310 315	961
tct ttc aat ctc aat gat aat ttc ttc acc gga gga tta cca gat gtc Ser Phe Asn Leu Asn Asp Asn Phe Phe Thr Gly Gly Leu Pro Asp Val 320 325 330	1009
gta gct ttg aat cct aat ctc gtt gaa ttc aaa atc ttc aac aac agt Val Ala Leu Asn Pro Asn Leu Val Glu Phe Lys Ile Phe Asn Asn Ser 335 340 345 350	1057
tcc acg ggg acg tta cca agg aat ctc ggg aaa ttc tca gaa atc tct Phe Thr Gly Thr Leu Pro Arg Asn Leu Gly Lys Phe Ser Glu Ile Ser 355 360 365	1105
gaa ttc gat gtc tcg acg aac aga ttc tcc ggt gaa ttg ccg ccg tat Glu Phe Asp Val Ser Thr Asn Arg Phe Ser Gly Glu Leu Pro Pro Tyr 370 375 380	1153
ttg tgc tac aga aga aaa ctt cag aag att atc acc ttc agc aat caa Leu Cys Tyr Arg Arg Lys Leu Gln Lys Ile Ile Thr Phe Ser Asn Gln 385 390 395	1201
tta agc ggc gaa att ccg gaa tct tac ggc gat tgt cat tcg ctt aat Leu Ser Gly Glu Ile Pro Glu Ser Tyr Gly Asp Cys His Ser Leu Asn 400 405 410	1249
tac att cgt atg gcg gat aac aaa ctc tcc ggc gaa gtt ccg gct agg Tyr Ile Arg Met Ala Asp Asn Lys Leu Ser Gly Glu Val Pro Ala Arg 415 420 425 430	1297
ttt tgg gaa ctt cct act cgt ctt gag cta gcc aac aac aat caa	1345

Phe Trp Glu Leu Pro Leu Thr Arg Leu Glu Leu Ala Asn Asn Asn Gln			
435	440	445	
tta caa ggt tcg att cct cct tcg att tcc aaa gct cgt cat cta tct			1393
Leu Gln Gly Ser Ile Pro Pro Ser Ile Ser Lys Ala Arg His Leu Ser			
450	455	460	
cag ctt gaa atc tcc gct aac aac ttc tcc ggt gtg att ccc gtc aaa			1441
Gln Leu Glu Ile Ser Ala Asn Asn Phe Ser Gly Val Ile Pro Val Lys			
465	470	475	
ctt tgt gat ctc cgt gat ctc aga gtc atc gat ctt agc cgc aac agt			1489
Leu Cys Asp Leu Arg Asp Leu Arg Val Ile Asp Leu Ser Arg Asn Ser			
480	485	490	
ttc tta gga tca att ccg tct tgc atc aac aaa ttg aag aat cta gag			1537
Phe Leu Gly Ser Ile Pro Ser Cys Ile Asn Lys Leu Lys Asn Leu Glu			
495	500	505	510
aga gta gag atg cag gag aac atg ctc gac ggc gag att ccg agt tca			1585
Arg Val Glu Met Gln Glu Asn Met Leu Asp Gly Glu Ile Pro Ser Ser			
515	520	525	
gtg agt tcg tgc acc gag tta acc gaa tta aat ctc tcc aac aac cgt			1633
Val Ser Ser Cys Thr Glu Leu Thr Glu Leu Asn Leu Ser Asn Asn Arg			
530	535	540	
tta cga ggc ggg ata cca ccg gaa ctc ggt gat tta ccg gtt tta aac			1681
Leu Arg Gly Gly Ile Pro Pro Glu Leu Gly Asp Leu Pro Val Leu Asn			
545	550	555	
tac ctg gat ctc tct aac aac caa ctc acc ggt gag att ccg gcg gag			1729
Tyr Leu Asp Leu Ser Asn Asn Gln Leu Thr Gly Glu Ile Pro Ala Glu			
560	565	570	
ctg ttg agg ctc aag ctt aat caa ttc aac gtc tcc gat aac aaa ctc			1777
Leu Leu Arg Leu Lys Leu Asn Gln Phe Asn Val Ser Asp Asn Lys Leu			
575	580	585	590
tat g gtaagattcc ttctggattt cagcaagata ttttcgacc cagtttctta g gt			1834
Tyr G ly			
aac ccg aat ctc tgt gcc cca aat ttg gat ccg att aga cct tgc cga			1882
Asn Pro Asn Leu Cys Ala Pro Asn Leu Asp Pro Ile Arg Pro Cys Arg			
595	600	605	
tcc aaa cgg gaa acc cgg tac att ctc cca atc tca atc ctc tgc atc			1930
Ser Lys Arg Glu Thr Arg Tyr Ile Leu Pro Ile Ser Ile Leu Cys Ile			
610	615	620	
gtt gca cta acc gga gct ttg gtt tgg cta ttc atc aaa acc aaa ccg			1978
Val Ala Leu Thr Gly Ala Leu Val Trp Leu Phe Ile Lys Thr Lys Pro			
625	630	635	640
tta ttc aag aga aaa ccg aaa cgg acc aac aaa ata acc atc ttc cag			2026
Leu Phe Lys Arg Lys Pro Lys Arg Thr Asn Lys Ile Thr Ile Phe Gln			
645	650	655	

228

229

aaa gtg aat gag aag agc gat gtc tat agc ttc ggg gtg gtt tta ctc	2761																																																																																																																
Lys Val Asn Glu Lys Ser Asp Val Tyr Ser Phe Gly Val Val Leu Leu																																																																																																																	
860	865	870		gaa ctg att acg gga aaa aga ccg aac gat tcg tct ttt ggg gag aat	2809	Glu Leu Ile Thr Gly Lys Arg Pro Asn Asp Ser Ser Phe Gly Glu Asn		875	880	885		aag gac att gtt aag ttt gca atg gaa gca gct ttg tgt tac cct tct	2857	Lys Asp Ile Val Lys Phe Ala Met Glu Ala Ala Leu Cys Tyr Pro Ser		890	895	900		cca tca gca gaa gac gga gcc atg aat caa gat tca ctt gga aac tat	2905	Pro Ser Ala Glu Asp Gly Ala Met Asn Gln Asp Ser Leu Gly Asn Tyr		905	910	915	920	cga gat ctt agc aag ctt gtt gat cca aag atg aaa ctt tcg acg aga	2953	Arg Asp Leu Ser Lys Leu Val Asp Pro Lys Met Lys Leu Ser Thr Arg		925	930	935		gag tat gaa gag ata gag aaa gtt ctt gac gtt gca ttg ctc tgt acg	3001	Glu Tyr Glu Glu Ile Glu Lys Val Leu Asp Val Ala Leu Leu Cys Thr		940	945	950		tcg tct ttt cct atc aac agg ccg acc atg agg aaa gta gta gag ttg	3049	Ser Ser Phe Pro Ile Asn Arg Pro Thr Met Arg Lys Val Val Glu Leu		955	960	965		ctt aaa gag aag aaa tca cta gag tga tattaatcct aggctttaa	3096	Leu Lys Glu Lys Lys Ser Leu Glu		970	975	ttattaggct tctataatgt aaaaaatccg actaggattt ttactcatta ttatagccat	3156	aggttggact ttgctttaaa gttt	3180	 		<210> 120		<211> 976		<212> PRT		<213> Arabidopsis thaliana		 		<400> 120		Met Leu Thr Asn Thr Asn Leu Phe Phe Phe Leu Ser Leu Leu Leu		1	5	10	15	 		Ser Cys Phe Leu Gln Val Ser Ser Asn Gly Asp Ala Glu Ile Leu Ser		20	25	30		 		Arg Val Lys Lys Thr Arg Leu Phe Asp Pro Asp Gly Asn Leu Gln Asp		35	40	45		 		Trp Val Ile Thr Gly Asp Asn Arg Ser Pro Cys Asn Trp Thr Gly Ile		50	55	60		 		Thr Cys His Ile Arg Lys Gly Ser Ser Leu Ala Val Thr Thr Ile Asp		65	70	75	80
870																																																																																																																	
gaa ctg att acg gga aaa aga ccg aac gat tcg tct ttt ggg gag aat	2809																																																																																																																
Glu Leu Ile Thr Gly Lys Arg Pro Asn Asp Ser Ser Phe Gly Glu Asn																																																																																																																	
875	880	885		aag gac att gtt aag ttt gca atg gaa gca gct ttg tgt tac cct tct	2857	Lys Asp Ile Val Lys Phe Ala Met Glu Ala Ala Leu Cys Tyr Pro Ser		890	895	900		cca tca gca gaa gac gga gcc atg aat caa gat tca ctt gga aac tat	2905	Pro Ser Ala Glu Asp Gly Ala Met Asn Gln Asp Ser Leu Gly Asn Tyr		905	910	915	920	cga gat ctt agc aag ctt gtt gat cca aag atg aaa ctt tcg acg aga	2953	Arg Asp Leu Ser Lys Leu Val Asp Pro Lys Met Lys Leu Ser Thr Arg		925	930	935		gag tat gaa gag ata gag aaa gtt ctt gac gtt gca ttg ctc tgt acg	3001	Glu Tyr Glu Glu Ile Glu Lys Val Leu Asp Val Ala Leu Leu Cys Thr		940	945	950		tcg tct ttt cct atc aac agg ccg acc atg agg aaa gta gta gag ttg	3049	Ser Ser Phe Pro Ile Asn Arg Pro Thr Met Arg Lys Val Val Glu Leu		955	960	965		ctt aaa gag aag aaa tca cta gag tga tattaatcct aggctttaa	3096	Leu Lys Glu Lys Lys Ser Leu Glu		970	975	ttattaggct tctataatgt aaaaaatccg actaggattt ttactcatta ttatagccat	3156	aggttggact ttgctttaaa gttt	3180	 		<210> 120		<211> 976		<212> PRT		<213> Arabidopsis thaliana		 		<400> 120		Met Leu Thr Asn Thr Asn Leu Phe Phe Phe Leu Ser Leu Leu Leu		1	5	10	15	 		Ser Cys Phe Leu Gln Val Ser Ser Asn Gly Asp Ala Glu Ile Leu Ser		20	25	30		 		Arg Val Lys Lys Thr Arg Leu Phe Asp Pro Asp Gly Asn Leu Gln Asp		35	40	45		 		Trp Val Ile Thr Gly Asp Asn Arg Ser Pro Cys Asn Trp Thr Gly Ile		50	55	60		 		Thr Cys His Ile Arg Lys Gly Ser Ser Leu Ala Val Thr Thr Ile Asp		65	70	75	80								
885																																																																																																																	
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